Playing board games, cognitive decline and dementia: a French population-based cohort study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-002998
Article Type:	Research
Date Submitted by the Author:	04-Apr-2013
Complete List of Authors:	Dartigues, Jean-Fran&#65533;ois; University of Bordeaux, Foubert, Alexandra; INSERM U 897, Epidemiology Le Goff, Mélanie; INSERM U 897, Epidemiology Viltard, Mélanie; Intitut for european expertise in Physiology, Amieva, Hélène; INSERM U 897, Epidemiology Orgogozo, Jean; INSERM U 897, Epidemiology Barberger-Gateau, Pascale; INSERM U 897, Epidemiology Helmer, Catherine; INSERM U 897, Epidemiology
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Neurology
Keywords:	Dementia < NEUROLOGY, Epidemiology < TROPICAL MEDICINE, PUBLIC HEALTH

Title : Playing board games, cognitive decline and dementia: a French population-based cohort study

Authors : Jean François Dartigues[1], Alexandra Foubert-Samier[1], Mélanie Le Goff[1], Mélanie Viltard[2], Hélène Amieva[1], Jean Marc Orgogozo[1], Pascale Barberger-Gateau[1], Catherine Helmer[1]

Adresses : 1 INSERM U 897, Université Bordeaux Ségalen, 146 rue Léo Saignat, 33076 Bordeaux cedex, France

2 IEEP, Institute for European expertise in physiology, 21, rue Leblanc 75015 Paris, France

Corresponding author : Jean François Dartigues, INSERM U 897, Université Bordeaux Ségalen, 146 rue Léo Saignat, 33076 Bordeaux cedex, France
Tel : +33 5 57571596 Fax : +33 5 57571486
Email : jfd@isped.u-bordeaux2.fr

Key words : Dementia, epidemiology, board games, risk factors, mediating factors

Word count : 2,846 words

Abstract

Objectives: To study the relationship between board game-playing and risk of subsequent dementia in the Paquid cohort.

Design: A prospective population-based study.

Setting: in the Bordeaux area South Western France.

Participants: 3,675 non-demented subjects at baseline.

Primary outcome measure: the risk of dementia during the twenty years of follow-up.

Results: Among 3,675 non-demented subjects at baseline, 32.2% reported regular board game playing. Eight hundred and forty subjects developed dementia during the twenty years of follow-up. The risk of dementia was fifteen per cent lower in board game players than in non-players (Hazard Ratio =0.85; 95% Confidence Interval = 0.74-0.99; p=0.04) after adjustment on age, gender, education and other confounders. The statistical significance disappeared after supplementary adjustment on baseline MMSE and depression (HR=0. 96; 95% CI = 0.82-1.12; p=0.61). However, board game players had less decline in their MMSE score during the follow-up of the cohort (β=0.011, p=0.03) and less incident depression than non-players (HR=0.84; 95%CI=0.72-0.98; p<0.03).

Conclusions: A possible beneficial effect of board game-playing on the risk of dementia could be mediated by less cognitive decline and less depression in elderly board game players.

Article summery

Article focus:

- Stimulating leisure activities are considered as possible protective factors against dementia and cognitive decline in elderly people, particularly due to enhancement of cognitive reserve.
- Previous papers have shown that playing games can improve cognitive performances in healthy elderly subject, but controversial results were obtained in dementia. Thus, playing board games could be a particularly relevant way to preserve cognition and to prevent cognitive decline or dementia, and could be recommended without any real drawbacks provided the favourable relationship between playing games and dementia is confirmed.
- However, to our knowledge, few authors have studied the relationship between playing board games and the risk of subsequent dementia in prospective cohort studies.

Key messages:

- Using the Paquid cohort data with 20 years of follow-up, we now show that board game players have a 15% lower risk of developing dementia than non-players.
- This reduced risk does not seem to be only a short-term effect as previously reported but is also a long-term effect with a reduction observed one or even two decades after the baseline collection of this popular leisure activity. However, in our study, the relationship disappeared after adjustment on baseline cognition and depression, which are known to be strong predictors of dementia.
- A possible beneficial effect of board game-playing on the risk of dementia could be mediated by less cognitive decline and less depression in elderly board game players.

Strengths and Limitations.

- With 20 years of follow-up, the Paquid cohort study is one of the longest duration of follow-up in the world for a population-based cohort.
- Because of the observational nature of our study, there is a possibility of residual or unmeasured confounding such as genetic factors.
- Although standard criteria and well-established procedures were used to make the diagnoses, misclassification is inevitable. Only reported regular activities were collected at baseline without direct measurement, although the history was checked by

informants whenever possible. We had no precise data on the frequency and duration of board game playing.

Stimulating leisure activities are considered as possible protective factors against dementia and cognitive decline in elderly people, particularly due to enhancement of cognitive reserve [1-2]. Cognitive reserve is considered as one of the major explanations for differences between individuals in susceptibility to age-related brain changes and pathology related to Alzheimer's Disease. Individuals with a large cognitive reserve can tolerate more of these changes than others and maintain their functions [1]. Playing board games is one of the most stimulating leisure activities for elderly people, even at an advanced age, and it has specific advantages compared to other games or activities. Playing board games is a recreational activity that promotes exposure to novelty, taking initiatives, planning, adaptation to winning or losing, and brings immediate pleasure to participants. In addition, playing games is an activity that can be undertaken with family members or friends and even with strangers, and it promotes social interaction and exchange with different generations. Furthermore, it is an inexpensive leisure activity that involves a wide range of tasks from simple ones as in bingo to complex ones as in bridge, and such games can be adapted to the level of the players. Finally, elderly people with physical disability, mild hearing or visual impairment can continue to participate in this stimulating leisure activity, irrespective of the season or the weather. Other stimulating leisure activities like reading, travelling, gardening, doing odd jobs or playing sports do not offer the same advantages and ease of practice. Thus, playing board games could be a particularly relevant way to preserve cognition and to prevent cognitive decline or dementia, and could be recommended without any real drawbacks provided the favourable relationship between playing games and dementia is confirmed.

Previous papers have shown that playing games can improve cognitive performances in healthy elderly subjects [3], but controversial results were obtained in mild cognitive impairment [4] or in dementia [5-6]. Playing games is known to enhance cognitive performances in working memory, executive function, semantic memory and logical reasoning [3 7-8]. However, to our knowledge, few authors have studied the relationship between playing board games and the risk of subsequent dementia in prospective cohort studies.

In a previous paper on the Paquid population-based cohort, we found that playing board games was significantly associated with a reduced risk of incident dementia three years later [9]. However, the results were obtained after a short follow-up and the significance disappeared after adjustment on cognitive performances at baseline. Similar results were obtained after 20 years of follow-up by Verghese et al in the Bronx Aging Study [10]. On the

contrary, in the MoVIES project, Hughes et al [11] studying different types of games found that only doing crossword puzzles was associated with a reduced risk of dementia while other games like bridge, other card games and other board games were not. Thus, the relationship remains uncertain and more evidence is needed to support preventive recommendations to elderly people about playing board games.

With the prolonged follow-up of the Paquid study with repeated measures of cognition, depression and clinical dementia, we re-analysed the relationship between playing board games collected at the baseline screening of the participants and the occurrence of dementia during the 20 years of follow-up of the cohort. Moreover, we analysed whether depression and cognitive decline before dementia could mediate the relationship between playing board games and dementia.

Methods

Study population

The data came from the Paquid cohort, an epidemiological prospective study on cerebral and functional aging with over 20 years of follow-up. The methodology has been previously described [12]. In brief, the initial baseline sample included 3,777 community dwellers, aged 65 or more, randomly selected from the electoral rolls in 75 different sites of two French administrative districts (Departments of Gironde and Dordogne). The participants were representative of the elderly community dwellers of the area in terms of age and sex. Since the baseline visit in 1988, the participants have been revisited at home by a dedicated neuropsychologist up to nine times over the entire follow-up. After 22 years, the Paquid cohort is still ongoing. The present analyses were conducted on the data collected over a 20-year period of follow-up.

Data collection

Leisure and social activities were collected at baseline by a standardized questionnaire during a face-to-face interview conducted by a psychologist. Ten activities were explored with the question: “Do you usually undertake this activity (at least once a week): yes or no?” The following activities were screened: reading, gardening, doing odd jobs or knitting, watching television, participating in sports, playing board games, looking after children, participating in group activities or associations, visiting friends or family members and travelling. Only playing board games was considered in this paper. Board games comprised card games, bingo, chess, draughts and other parlour games.

A neuropsychological battery was conducted at baseline and at each follow-up visit with assessment of visual memory, verbal memory, language, executive function and simple logical reasoning [12]. A French version of the Mini-Mental Status Examination (MMSE) [13] was used as an index of global cognitive performance. Scores range from 0 to 30. Depressive symptomatology was assessed at each follow-up screening using the French version of the Centre for Epidemiological Studies Depression Scale (CES-D) [14]. This is a 20-item self-report scale developed for use in epidemiological studies in the community. Scores range from 0 to 60 according to the frequency of the depressive symptoms during the previous week. According to a previous validation study for the French population, CES-D cut-off scores of 17 for men and 23 for women indicate clinically relevant depression [14]. Subjects were considered as having depression if they were treated by anti-depressors or had a score above the cut-off score at the CESD.

At baseline and at each follow-up visit, after the neuropsychological evaluation, the neuropsychologist filled in the Diagnostic and Statistical Manual of Mental Disorders 3rd ed. revised (DSM-IIIR) to identify subjects suspected of being demented. These cases and those with at least a three-point decline in MMSE score since the previous visit were examined at home by a neurologist to confirm or not the diagnosis of dementia and specify the etiology. All diagnoses of dementia were assigned at a case consensus conference attended by the study neurologist and two other dementia specialists according to the DSM-IIIR criteria. When evaluating cognitive status, the members of the consensus conference had no knowledge of leisure activities practiced by subjects.

Statistical analyses

Descriptive and comparative analyses were conducted using appropriate tests (*t*-test or chi-square test). Kaplan-Meier curves for the risk of incident dementia were obtained for the two categories of subjects according to their board game playing and compared with the Log Rank test.

To estimate the risk of dementia associated with game-playing, incident cases of dementia occurring between the baseline screening and the 20th year of follow-up were considered as an outcome variable. The time-to-event was defined as the time from baseline to the date of a diagnosis of dementia or to the last follow-up for subjects without dementia. Participants were censored at the time of diagnosis of dementia or at the last follow-up for those non-demented. Adjustment on possible confounders was performed with the multivariate Cox proportional hazards model with delayed entry taking age as time scale**.** The

multivariate model included the following covariates: gender, educational level (subjects were considered higher educated if they had obtained the French primary school certificate corresponding to about seven years of schooling), marital status, self-reported diabetes and stroke (model 1). Supplementary adjustment was made on self-reported visual and hearing impairment.

We examined the influence of baseline cognitive performances on the MMSE score and the presence of depression at baseline (model 2). Risk of cognitive decline was analysed by a multivariate mixed model taking repeated values of the MMSE score during the 20 years of follow-up as outcome. Beta transformation of the MMSE score was used to take into account the ceiling effect of the test in non-demented cases [15]. Board game playing was considered as covariate with adjustment on confounders as in the previous multivariate model.

To estimate the risk of incident depression associated with board game-playing, incident cases of depression occurring between the baseline screening and the 20th year of follow-up were considered as the outcome variable. The time-to-event was defined as the time from baseline to the date of a diagnosis of depression or to the last follow-up for subjects without depression. Participants were censored at the time of the first diagnosis of depression during the follow-up or at the last follow-up for those never depressed over the follow-up. Adjustment on possible confounders was performed with the multivariate Cox proportional hazards model using the same adjustments as previously**.**

The analyses were performed using SAS, version 9.2 (SAS Institute, Inc., Cary, NC).

Results

Characteristics of board game players

Among the 3,777 participants, 102 (2.7%) were classified as prevalent cases of dementia at the baseline screening and excluded from the sample. Of the remaining 3675 subjects, five had missing data for board game playing (0.1%). One thousand one hundred and eighty-one subjects reported regular board game playing (32.2%). Board game players were younger, more educated, more often married, less depressed and had better cognitive performances at baseline screening than non-players (Table 1). However, the proportion of board game players remained high in very old age (18% in subjects aged from 85 to 89 years, and even 12.5% in those older than 89 years), and even in non-demented subjects with low cognitive performances (18.8% in subjects with an MMSE between 20 and 23, 10.6% in subjects with an MMSE lower than 20).

Table 1. Characteristics of participants according to board game playing. Paquid Study n=3670

	Players (n=1181)	Non-players (n=2489)*	p value
Gender (males)	501 (42.4)	1039 (41.7)	0.70
Age at inclusion (years): mean (SD)	73.6 (5.9)	76.0 (7.1)	<0.0001
Educational Level (higher)	879 (74.4)	1513 (60.8)	<0.0001
Marital Status			0.0305
Married	708 (59.9)	1394 (56.0)	
Widowed	381 (32.3)	905 (36.4)	
Single	52 (4.4)	127 (5.1)	
Divorced	40 (3.4)	63 (2.5)	
Diabetes	87 (7.4)	219 (8.8)	0.14
Stroke	42 (3.6)	152 (6.1)	0.0012
MMSE score at inclusion: mean (SD)	26.9 (2.6)	25.3 (3.6)	<0.0001
Depression at inclusion	116 (9.9)	494 (20.4)	<0.0001

Unless otherwise stated values are numbers (%)

SD: Standard Deviation

Board game-playing and risk of incident dementia

Among the 3670 participants, 2987 (81.4%) were seen again at least once during the twenty years of follow-up. One hundred and forty-two persons deceased before the first screening (3.9%) and 541 refused to participate or were lost to follow-up (14.7%). The proportion of board game players was greater in those who were followed-up at least once.

Eight hundred and thirty cases of incident dementia (27.8%) were observed during the twenty years of follow-up. The cumulative risk of dementia was significantly reduced in subjects board game players versus non-players (Log rank test = 24.2, p<0.001). After three years of follow-up, 3% of board players developed dementia versus 6% of non-players, 16% versus 27% after ten years and 47% versus 58% after twenty years (Figure 1).

After adjustment on age, gender, education, marital status, history of stroke and diabetes (Table 2), the risk of dementia remained significantly reduced (HR = 0.85, 95%CI= 0.74-0.99, p=0.04). The relationship remained unchanged after supplementary adjustment on visual and hearing impairment. However, the relationship was no longer significant after

supplementary adjustment on depression and MMSE score at baseline (HR=0.96, 95%CI=0.82-1.12, p=0.61). In the latter model, depression (HR=1.34, 95%CI=1.12-1.60, p=0.0011) and MMSE score at baseline (for one point fewer HR=1.10, 95%CI=1.08-1.12, p<0.0001) were strong predictors of dementia.

Table 2. Risk of dementia according to board game playing in the Paquid cohort. Multivariate Cox model.

	Model 1*			Model 2**		
	HR	95%CI	p Value	HR	95%CI	p Value
Board game (players vs non-players)	0.85	0.74-0.99	0.04	0.96	0.82-1.12	0.61
Gender (female vs male)	1.33	1.13-1.56	0.0007	1.26	1.06-1.48	0.0076
Education (higher vs lower)	0.61	0.53-0.70	<0.0001	0.83	0.71-0.98	0.03
marital status						
widowed vs married	0.90	0.76-1.05	0.18	0.85	0.72-1.00	0.05
single vs married	1.25	0.92-1.71	0.16	1.19	0.85-1.66	0.31
divorced vs married	1.13	0.76-1.70	0.54	1.06	0.70-1.60	0.80
history of stroke (yes vs no)	1.57	1.19-2.08	0.0016	1.32	0.97-1.79	0.07
Diabetes (yes vs no)	1.12	0.85-1.48	0.42	1.06	0.80-1.42	0.67
MMSE score				0.91	0.89-0.93	<0.0001
Depression (yes vs no)				1.34	1.12-1.60	0.0011

* Adjustment on age, gender, education, marital status, history of stroke and diabetes

** Adjustment on age, gender, education, marital status, history of stroke, diabetes, MMSE score and depression

Board game-playing, cognitive decline and risk of incident depression

Board game players had less cognitive decline in MMSE score than non-players after adjustment on age, gender, education, marital status, history of stroke and diabetes (β=0.011, p=0.03). The relationship remained unchanged after supplementary adjustment on depression at baseline (β=0.010, p=0.04).

Among the 2987 participants, 2464 were classified as non-depressed at baseline. Of those, 718 developed incident depression (29.1%) during the 20 years of follow-up. The risk of incident depression was significantly reduced in board game players after adjustment on

age, gender, education, marital status, history of stroke and diabetes (HR=0.84; 95%CI=0.72-0.98; p<0.03). This relationship remained almost unchanged but was only borderline significant after adjustment on MMSE score at baseline screening (HR=0.87; 95%CI=0.74-1.02; p=0.08).

Discussion

Playing board games is a common stimulating leisure activity in elderly French people since one third of subjects older than 65 in the general population reported regularly practising it. The rate of such activity remained high even in very old age and in subjects with cognitive deficit. Using the Paquid cohort data with 20 years of follow-up, which is one of the longest duration of follow-up in the world for a population-based cohort, we now show that board game players have a 15% lower risk of developing dementia than non-players. This reduced risk does not seem to be only a short-term effect as previously reported [9] but is also a long-term effect with a reduction observed one or even two decades after the baseline collection of this popular leisure activity. The association between board game playing and the risk of dementia remained robust after adjustment on confounding variables such as age, gender, educational level, marital status, and presence or absence of stroke or diabetes.

Our results are in accordance with findings from the Bronx Aging Cohort [10] conducted in a different population in the USA. However, in our study, the relationship disappeared after adjustment on baseline cognition and depression, which are known to be strong predictors of dementia. This means that the reduced risk of dementia could be related to the fact that board game players had better cognitive performances and were less depressed at baseline screening than non-players. On the contrary, baseline MMSE score and depression appeared to be significantly related to the subsequent risk of dementia.

To test whether cognitive decline and the occurrence of depression were mediating factors in the relationship between playing board games and dementia, we studied non-demented subjects with regard to the risk of cognitive decline and incident depression in board game players versus non-players. Board game players had significantly less cognitive decline and less incident depression than non-players. Thus, cognitive decline and depression have the three statistical conditions to be considered as mediating factors [16]: cognitive decline and depression were associated with an increased risk of dementia; board game playing was associated with a reduced risk of cognitive decline and depression; and after multivariate analysis, playing board games was no longer significantly associated with dementia, unlike MMSE score and depression at baseline. This means that playing board

games seems to have a favourable effect on cognition and depression before dementia and could therefore have a favourable effect on the risk of dementia. Of course, we cannot exclude that an unmeasured cognitive decline before baseline could precede the discontinuation of board game playing. The relationship could be bidirectional. Only repeated measures of board game playing along with repeated measures of depression and cognition could disentangle this relationship.

Several explanations could be given to explain the relationship between board game playing, cognitive decline, depression and then dementia. Less board game playing might be an early marker or an early consequence of dementia that precedes the decline in MMSE score and the occurrence of depression before dementia. Another explanation could be that board game playing is a marker of behaviour that promotes successful aging, and that this could be the real non-specific factor protecting against cognitive decline, depression and then dementia [17].

Alternatively, board game playing might increase or preserve cognitive reserve, thereby delaying the clinical onset of dementia [1] or slowing the pathological process of the disease [10].

Because of the observational nature of our study, there is a possibility of residual or unmeasured confounding. For example, we did not adjust on genetic factors, which are available only in a small number of the Paquid subjects. However, to our knowledge, there is no evidence showing that APOE4 carriers play board game less than non-carriers, and there is no obvious plausible biological explanation for such an association. The observed association between board game playing and dementia appears to be independent from educational level and marital status, which may influence people's involvement in board game playing.

Our study has other limitations. Although standard criteria and well-established procedures were used to make the diagnoses, misclassification is inevitable. Only reported regular activities were collected at baseline without direct measurement, although the history was checked by informants whenever possible. We had no precise data on the frequency and duration of board game playing. The refusal rate during the follow-up of the cohort was quite low, but many more subjects died than became demented. However, the risk of death was lower in players than in non-players. Even if a competitive risk between death and dementia might occur, it would lead to an underestimation of the risk of dementia in non-players.

Although this epidemiological study suggests that playing board games has a protective effect on cognitive decline, depression and then dementia, the evidence is not definitive. Only controlled studies could truly establish whether playing board games is

beneficial and could rule out a reverse causation. However, such a trial appears almost impossible to organize without the possibility of blinding. Even if the evidence is not completely documented, the immediate pleasure procured by playing board games, the advantages that social interaction offers and the ease of applying such a measure in the real world without any drawbacks mean that this activity could be promoted for successful aging.

The present findings, which replicate those obtained with another cohort study in a different elderly population, suggest recommending board game playing in old age to reduce the risk of cognitive decline and depression, and in turn to reduce the risk of dementia.

Acknowledgments and Funding The Paquid study was founded by Novartis pharma, IPSEN pharma, Conseil Régional d'Aquitaine and Institute for European expertise in physiology

Competing interests No competing interests

Contributorship statement

JFD was involved in the design, data collection, analysis, he advised on data interpretation and wrote the initial draft. AFS was involved in analysis and she advised on data interpretation. MLG was involved in data collection, analysis and she advised on data interpretation. MV advised on data interpretation. HA was involved in the design and data collection. JMO was involved in the design and data collection. PBG was involved in design and data collection. CM was involved in design, data collection, analysis and she advised on data interpretation. All authors read and approved the final manuscript.

Patient consent Obtained

Ethics approval Ethics approval was provided by the Bordeaux 2 University Ethics Committee in 1988.

Data Sharing JF Dartigues declare that the data for this article are available if required.

References

1 Stern Y. Cognitive reserve in ageing and Alzheimer's disease. Lancet neurology 2012 **11**:1006-12.
2 Akbaraly TN, Portet F, Fustinoni S, et al. Leisure activities and the risk of dementia in the elderly: results from the Three-City Study. Neurology 2009;**73**:854-61.
3 Stern Y, Blumen HM, Rich LW, et al. Space Fortress game training and executive control in older adults: a pilot intervention. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 2011;**18**:653-77.
4 Barnes DE, Yaffe K, Belfor N, et al. Computer-based cognitive training for mild cognitive impairment: results from a pilot randomized, controlled trial. Alzheimer Dis Assoc Disord 2009;**23**:205-10.
5 Cohen GD, Firth KM, Biddle S, et al. The first therapeutic game specifically designed and evaluated for Alzheimer's disease. Am J Alzheimers Dis Other Demen 2008;**23**:540-51.
6 Bosch-Domenech A, Nagel R, Sanchez-Andres JV. Prosocial capabilities in Alzheimer's patients. J Gerontol B Psychol Sci Soc Sci 2010;**65B**:119-28.
7 Clarkson-Smith L, Hartley AA. The game of bridge as an exercise in working memory and reasoning. J Gerontol 1990;**45**:P233-8.
8 Nouchi R, Taki Y, Takeuchi H, et al. Brain training game improves executive functions and processing speed in the elderly: a randomized controlled trial. PLoS One 2012;**7**:e29676.
9 Fabrigoule C, Letenneur L, Dartigues JF, et al. Social and leisure activities and risk of dementia: a prospective longitudinal study. J Am Geriatr Soc 1995;**43**:485-90.
10 Verghese J, Lipton RB, Katz MJ, et al. Leisure activities and the risk of dementia in the elderly. N Engl J Med 2003;**348**:2508-16.
11 Hughes TF, Chang CC, Vander Bilt J, et al. Engagement in reading and hobbies and risk of incident dementia: the MoVIES project. Am J Alzheimers Dis Other Demen 2010;**25**:432-8.
12 Dartigues JF, Gagnon M, Michel P, et al. [The Paquid research program on the epidemiology of dementia. Methods and initial results]. Rev Neurol (Paris) 1991;**147**:225-30.
13 Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;**12**:189-98.
14 Fuhrer R, Antonucci TC, Gagnon M, et al. Depressive symptomatology and cognitive functioning: an epidemiological survey in an elderly community sample in France. Psychol Med 1992;**22**:159-72.
15 Proust-Lima C, Dartigues JF, Jacqmin-Gadda H. Misuse of the linear mixed model when evaluating risk factors of cognitive decline. Am J Epidemiol 2011;**174**:1077-88.
16 Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. J Pers Soc Psychol 1986;**51**:1173-82.
17 Dartigues JF, Feart C. Risk factors for Alzheimer disease: aging beyond age? Neurology 2011;**77**:206-7.

Figure 1. Probability of survival without dementia according to regular board game playing. Kaplan Meier Estimates.

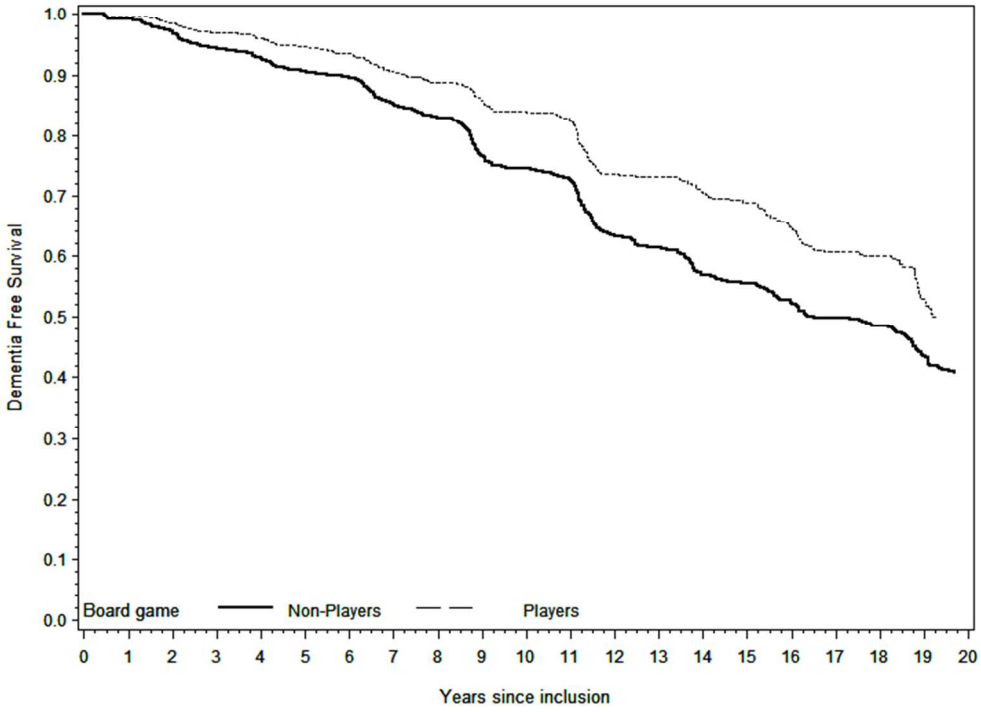

Figure 1. Probability of survival without dementia according to regular board game playing. Kaplan Meier Estimates.
184x151mm (100 x 100 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

Please fill out the page numbers on this form and upload the file as a supplemental file when you submit your revision

Manuscript Number_____

	Item No	Recommendation	Indicate page number ↓ (Or n/a if not applicable)
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	5-6
		(*c*) Explain how missing data were addressed	NA
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6-7
		(b) Indicate number of participants with missing data for each variable of interest	6
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	7
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA
		Cross-sectional study—Report numbers of outcome events or summary measures	NA
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95%	8-9

		confidence interval). Make clear which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ open

Playing board games, cognitive decline and dementia: a French population-based cohort study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-002998.R1
Article Type:	Research
Date Submitted by the Author:	26-Jun-2013
Complete List of Authors:	Dartigues, Jean-Fran&#65533;ois; University of Bordeaux, Foubert, Alexandra; INSERM U 897, Epidemiology Le Goff, Mélanie; INSERM U 897, Epidemiology Viltard, Mélanie; Intitut for european expertise in Physiology, Amieva, Hélène; INSERM U 897, Epidemiology Orgogozo, Jean; INSERM U 897, Epidemiology Barberger-Gateau, Pascale; INSERM U 897, Epidemiology Helmer, Catherine; INSERM U 897, Epidemiology
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Neurology
Keywords:	Dementia < NEUROLOGY, Epidemiology , PUBLIC HEALTH

Title : Playing board games, cognitive decline and dementia: a French population-based cohort study

Authors : Jean François Dartigues[1], Alexandra Foubert-Samier[1], Mélanie Le Goff[1], Mélanie Viltard[2], Hélène Amieva[1], Jean Marc Orgogozo[1], Pascale Barberger-Gateau[1], Catherine Helmer[1]

Adresses : 1 INSERM U 897, Université Bordeaux Ségalen, 146 rue Léo Saignat, 33076 Bordeaux cedex, France

2 IEEP, Institute for European expertise in physiology, 21, rue Leblanc 75015 Paris, France

Corresponding author : Jean François Dartigues, INSERM U 897, Université Bordeaux Ségalen, 146 rue Léo Saignat, 33076 Bordeaux cedex, France
Tel : +33 5 57571596 Fax : +33 5 57571486
Email : jfd@isped.u-bordeaux2.fr

Key words : Dementia, epidemiology, board games, risk factors, mediating factors

Word count : 2,846 words

Abstract

Objectives: To study the relationship between board game-playing and risk of subsequent dementia in the Paquid cohort.

Design: A prospective population-based study.

Setting: in the Bordeaux area in South Western France.

Participants: 3,675 non-demented subjects at baseline.

Primary outcome measure: the risk of dementia during the twenty years of follow-up.

Results: Among 3,675 non-demented subjects at baseline, 32.2% reported regular board game playing. Eight hundred and forty subjects developed dementia during the twenty years of follow-up. The risk of dementia was fifteen per cent lower in board game players than in non-players (Hazard Ratio =0.85; 95% Confidence Interval = 0.74-0.99; p=0.04) after adjustment on age, gender, education and other confounders. The statistical significance disappeared after supplementary adjustment on baseline MMSE and depression (HR=0. 96; 95% CI = 0.82-1.12; p=0.61). However, board game players had less decline in their MMSE score during the follow-up of the cohort (β=0.011, p=0.03) and less incident depression than non-players (HR=0.84; 95%CI=0.72-0.98; p<0.03).

Conclusions: A possible beneficial effect of board game-playing on the risk of dementia could be mediated by less cognitive decline and less depression in elderly board game players.

Article summery

Article focus:

- Stimulating leisure activities are considered as possible protective factors against dementia and cognitive decline in elderly people, particularly due to enhancement of cognitive reserve.
- Previous papers have shown that playing games can improve cognitive performances in healthy elderly subject, but controversial results were obtained in dementia. Thus, playing board games could be a particularly relevant way to preserve cognition and to prevent cognitive decline or dementia, and could be recommended without any real drawbacks provided the favourable relationship between playing games and dementia is confirmed.
- However, to our knowledge, few authors have studied the relationship between playing board games and the risk of subsequent dementia in prospective cohort studies.

Key messages:

- Using the Paquid cohort data with 20 years of follow-up, we now show that board game players have a 15% lower risk of developing dementia than non-players.
- This reduce risk does not seem to be only a short-term effect as previously reported but is also a long-term effect with a reduction observed one or even two decades after baseline collection of this popular leisure activity. However, in our study, the relationship disappeared after adjustment on baseline cognition and depression, which are known to be strong predictors of dementia.
- A possible beneficial effect of board game-playing on the risk of dementia could be mediated by less cognitive decline and less depression in elderly board game players.

Strengths and limitations:

- With 20 years of follow-up, the Paquid cohort study is one of the longest duration of follow-up in the world for a population-based cohort.
- Because of the observational nature of our study, there is a possibility of residual or unmeasured confounding such as genetic factors.
- Although standard criteria and well-established procedures were used to make the diagnoses, misclassification is inevitable. Only reported regular activities were collected at baseline without direct measurement, although the history was checked by

informants whenever possible. We had no precise data on the frequency and duration of board game playing.

Stimulating leisure activities are considered as possible protective factors against dementia and cognitive decline in elderly people, particularly due to enhancement of cognitive reserve [1-2]. Cognitive reserve is considered as one of the major explanations for differences between individuals in susceptibility to age-related brain changes and pathology related to Alzheimer's disease. Individuals with a large cognitive reserve can tolerate more of these changes than others and maintain their functions [1]. Playing board games is one of the most stimulating leisure activities for elderly people, even at an advanced age, and it has specific advantages compared to other games or activities. Playing board games is a recreational activity that promotes exposure to novelty, taking initiatives, planning, adaptation to winning or losing, and brings immediate pleasure to participants. In addition, playing games is an activity that can be undertaken with family members or friends and even with strangers, and it promotes social interaction and exchange with different generations. Furthermore, it is an inexpensive leisure activity that involves a wide range of tasks from simple ones as in bingo to complex ones as in bridge, and such games can be adapted to the level of the players. Finally, elderly people with physical disability, mild hearing or visual impairment can continue to participate in this stimulating leisure activity, irrespective of the season or the weather. Other stimulating leisure activities like reading, travelling, gardening, doing odd jobs or playing sports do not offer the same advantages and ease of practice. Thus, playing board games could be a particularly relevant way to preserve cognition and to prevent cognitive decline or dementia, and could be recommended without any real drawbacks provided the favourable relationship between playing games and dementia is confirmed.

Previous papers have shown that playing games can improve cognitive performances in healthy elderly subjects [3], but controversial results were obtained in mild cognitive impairment [4] or in dementia [5-6]. Playing games is known to enhance cognitive performances in working memory, executive function, semantic memory and logical reasoning [3, 7-8]. However, to our knowledge, few authors have studied the relationship between playing board games and the risk of subsequent dementia in prospective cohort studies.

In a previous paper on the Paquid population-based cohort, we found that playing board games was significantly associated with a reduced risk of incident dementia three years later [9]. However, the results were obtained after a short follow-up and the significance disappeared after adjustment on cognitive performances at baseline. Similar results were obtained after 20 years of follow-up by Verghese et al in the Bronx Aging Study [10]. On the

contrary, in the MoVIES project, Hughes et al [11] studying different types of games found that only doing crossword puzzles was associated with a reduced risk of dementia while other games like bridge, other card games and other board games were not. Thus, the relationship remains uncertain and more evidence is needed to support preventive recommendations to elderly people about playing board games.

With the prolonged follow-up of the Paquid study with repeated measures of cognition, depression and clinical dementia, we re-analysed the relationship between playing board games collected at the baseline screening of the participants and the occurrence of dementia during the 20 years of follow-up of the cohort. Moreover, we analysed whether depression and cognitive decline before dementia could mediate the relationship between playing board games and dementia.

Methods

Study population

The data came from the Paquid cohort, an epidemiological prospective study on cerebral and functional aging with over 20 years of follow-up. The methodology has been previously described [12]. In brief, the initial baseline sample included 3,777 community dwellers, aged 65 or more, randomly selected from the electoral rolls in 75 different sites of two French administrative districts (Departments of Gironde and Dordogne). The participants were representative of the elderly community dwellers of the area in terms of age and sex. Since the baseline visit in 1988, the participants have been revisited at home by a dedicated neuropsychologist up to nine times over the entire follow-up. After 22 years, the Paquid cohort is still ongoing. The present analyses were conducted on the data collected over a 20-year period of follow-up.

Data collection

Leisure and social activities were collected at baseline by a standardized questionnaire during a face-to-face interview conducted by a psychologist. Ten activities were explored with the question: “Do you usually undertake this activity (at least once a week): yes or no?” The following activities were screened: reading, gardening, doing odd jobs or knitting, watching television, participating in sports, playing board games, looking after children, participating in group activities or associations, visiting friends or family members and travelling. Only playing board games was considered in this paper. Board games comprised card games, bingo, chess, draughts and other parlour games.

A neuropsychological battery was conducted at baseline and at each follow-up visit with assessment of visual memory, verbal memory, language, executive function and simple logical reasoning [12]. A French version of the Mini-Mental State Examination (MMSE) [13] was used as an index of global cognitive performance. Scores range from 0 to 30. Depressive symptomatology was assessed at each follow-up screening using the French version of the Centre for Epidemiological Studies Depression Scale (CES-D) [14]. This is a 20-item self-report scale developed for use in epidemiological studies in the community. Scores range from 0 to 60 according to the frequency of the depressive symptoms during the previous week. According to a previous validation study for the French population, CES-D cut-off scores of 17 for men and 23 for women indicate clinically relevant depression [14]. Subjects were considered as having depression if they were treated by anti-depressors or had a score above the cut-off score at the CESD.

At baseline and at each follow-up visit, after the neuropsychological evaluation, the neuropsychologist filled in the Diagnostic and Statistical Manual of Mental Disorders 3rd ed. revised (DSM-IIIR) to identify subjects suspected of being demented. These cases and those with at least a three-point decline in MMSE score since the previous visit were examined at home by a neurologist to confirm or not the diagnosis of dementia and specify the etiology. All diagnoses of dementia were assigned at a case consensus conference attended by the study neurologist and two other dementia specialists according to the DSM-IIIR criteria. When evaluating cognitive status, the members of the consensus conference had no knowledge of leisure activities practiced by subjects.

Statistical analyses

Descriptive and comparative analyses were conducted using appropriate tests (*t*-test or chi-square test). Kaplan-Meier curves for the risk of incident dementia were obtained for the two categories of subjects according to their board game playing and compared with the Log Rank test.

To estimate the risk of dementia associated with game-playing, incident cases of dementia occurring between the baseline screening and the 20th year of follow-up were considered as an outcome variable. The time-to-event was defined as the time from baseline to the date of a diagnosis of dementia or to the last follow-up for subjects without dementia. Participants were censored at the time of diagnosis of dementia or at the last follow-up for those non-demented. Adjustment on possible confounders was performed with the multivariate Cox proportional hazards model with delayed entry taking age as time scale**.** The

multivariate model included the following covariates: gender, educational level (classified in five levels: high school, college, secondary level, primary school with diploma, primary school without diploma or no schooling), marital status, self-reported diabetes and stroke (model 1). Supplementary adjustment was made on self-reported visual, hearing impairment and ApoE 4 genotype on the subsample of the cohort with blood sampling (n=623).

We examined the influence of baseline cognitive performances on the MMSE score and the presence of depression at baseline (model 2). Risk of cognitive decline was analysed by a multivariate mixed model taking repeated values of the MMSE score during the 20 years of follow-up as outcome. Beta transformation of the MMSE score was used to take into account the ceiling effect of the test in non-demented cases [15]. Board game playing was considered as covariate with adjustment on confounders as in the previous multivariate model.

To estimate the risk of incident depression associated with board game-playing, incident cases of depression occurring between the baseline screening and the 20th year of follow-up were considered as the outcome variable. The time-to-event was defined as the time from baseline to the date of a diagnosis of depression or to the last follow-up for subjects without depression. Participants were censored at the time of the first diagnosis of depression during the follow-up or at the last follow-up for those never depressed over the follow-up. Adjustment on possible confounders was performed with the multivariate Cox proportional hazards model using the same adjustments as previously**.**

The analyses were performed using SAS, version 9.2 (SAS Institute, Inc., Cary, NC).

Results

Characteristics of board game players

Among the 3,777 participants, 102 (2.7%) were classified as prevalent cases of dementia at the baseline screening and excluded from the sample. Of the remaining 3675 subjects, five had missing data for board game playing (0.1%). One thousand one hundred and eighty-one subjects reported regular board game playing (32.2%). Board game players were younger, more educated, more often married, less depressed and had better cognitive performances at baseline screening than non-players (Table 1). However, the proportion of board game players remained high in very old age (18% in subjects aged from 85 to 89 years, and even 12.5% in those older than 89 years), and even in non-demented subjects with low cognitive performances (18.8% in subjects with an MMSE between 20 and 23, 10.6% in subjects with an MMSE lower than 20). In the subsample of 623 subjects with blood sampling

the proportion of ApoE 4 carriers was the same in both groups (23.5% for non-players vs 21.2 for players %, p=0.5).

Table 1. Characteristics of participants according to board game playing. Paquid Study n=3670

	Players (n=1181)	Non-players (n=2489)	p value
Gender (males)	501 (42.4)	1039 (41.7)	0.70
Age at inclusion (years): mean (SD)	73.6 (5.9)	76.0 (7.1)	<0.0001
Educational Level (higher)			
Primary school without diploma or no schooling	302 (25.6)	976 (39.2)	
Primary school with diploma	546 (46.2)	1058 (42.5)	
Secondary level	179 (15.2)	228 (9.2)	<0.0001
College	77 (6.5)	127 (5.1)	
High school	77 (6.5)	100 (4.0)	
Marital Status			0.0305
Married	708 (59.9)	1394 (56.0)	
Widowed	381 (32.3)	905 (36.4)	
Single	52 (4.4)	127 (5.1)	
Divorced	40 (3.4)	63 (2.5)	
Diabetes	87 (7.4)	219 (8.8)	0.14
Stroke	42 (3.6)	152 (6.1)	0.0012
MMSE score at inclusion: mean (SD)	26.9 (2.6)	25.3 (3.6)	<0.0001
Depression at inclusion	116 (9.9)	494 (20.4)	<0.0001
ApoE 4 genotype (carriers)*	48 (21.2)	93 (23.5)	0.5

Unless otherwise stated values are numbers (%)

SD: Standard Deviation

* n= 623 (396 non-players and 227 players)

Board game-playing and risk of incident dementia

Among the 3670 participants, 2987 (81.4%) were seen again at least once during the twenty years of follow-up. One hundred and forty-two persons deceased before the first screening (3.9%) and 541 refused to participate or were lost to follow-up (14.7%). The proportion of board game players was greater in those who were followed-up at least once.

Eight hundred and thirty cases of incident dementia (27.8%) were observed during the twenty years of follow-up. The cumulative risk of dementia was significantly reduced in subjects board game players versus non-players (Log rank test = 24.2, p<0.001). After three years of follow-up, 3% of board players developed dementia versus 6% of non-players, 16% versus 27% after ten years and 47% versus 58% after twenty years (Figure 1).

After adjustment on age, gender, education, marital status, history of stroke and diabetes (Table 2), the risk of dementia remained significantly reduced (HR = 0.85, 95%CI= 0.74-0.99, p=0.04). The relationship remained unchanged after supplementary adjustment on visual and hearing impairment. However, the relationship was no longer significant after supplementary adjustment on depression and MMSE score at baseline (HR=0.96, 95%CI=0.82-1.12, p=0.61). In the latter model, depression (HR=1.34, 95%CI=1.12-1.60, p=0.0011) and MMSE score at baseline (for one point fewer HR=1.10, 95%CI=1.08-1.12, p<0.0001) were strong predictors of dementia. In supplementary analyses, we found that after separated adjustment on MMSE and depression, the significant relationships between board game playing and dementia disappeared in both analyses, but most of the effect seems to be due to controlling for MMSE.

Finally, we made a supplementary adjustment on ApoE 4 genotype on a subsample of the Paquid cohort of 618 subjects. In this subsample of subjects, after adjustment on ApoE 4 genotype (carriers vs no carriers), the HR for dementia related to playing board game decreased to 0.74 but was no more significant (p=0.06).

Table 2. Risk of dementia according to board game playing in the Paquid cohort. Multivariate Cox model.

	Model 1*			Model 2**		
	HR	95%CI	p Value	HR	95%CI	p Value
Board game (players vs non-players)	0.85	0.74-0.99	0.04	0.96	0.82-1.13	0.62
Gender (female vs male)	1.29	1.10-1.52	0.002	1.23	1.04-1.46	0.01
Education (higher vs lower)						
Primary school with diploma	0.65	0.56-0.76	<0.0001	0.85	0.72-1.01	0.07
Secondary level	0.58	0.45-0.74	<0.0001	0.84	0.64-1.11	0.22
College	0.50	0.36-0.71	0.0001	0.76	0.53-1.09	0.13
High school	0.38	0.25-0.58	<0.0001	0.57	0.37-0.88	0.01
marital status						
widowed vs married	0.89	0.76-1.05	0.16	0.85	0.72-1.00	0.05
single vs married	1.28	0.93-1.75	0.12	1.20	0.86-1.68	0.28
divorced vs married	1.16	0.77-1.74	0.49	1.06	0.70-1.61	0.78
history of stroke (yes vs no)	1.55	1.17-2.05	0.0016	1.31	0.97-1.78	0.08
Diabetes (yes vs no)	1.10	0.84-1.46	0.48	1.05	0.79-1.40	0.72
MMSE score				0.91	0.89-0.93	<0.0001
Depression (yes vs no)				1.34	1.12-1.59	0.001

* Adjustment on age, gender, education, marital status, history of stroke and diabetes

** Adjustment on age, gender, education, marital status, history of stroke, diabetes, MMSE score and depression

Board game-playing, cognitive decline and risk of incident depression

Board game players had less cognitive decline in MMSE score than non-players after adjustment on age, gender, education, marital status, history of stroke and diabetes (β=0.011, p=0.03). The relationship remained unchanged after supplementary adjustment on depression at baseline (β=0.010, p=0.04). The cognitive decline may begin several years before the diagnosis of dementia as showed by us [16]. To explore a possible reverse causation, we studied the relationship between board game playing and the cognitive decline, eliminating those who became demented over the first 10 years of follow-up and over the entire period.

The beta coefficients slightly decrease (from 0.01 to 0.008) but become non significant (respectively p=0.07 and p=0.15).

Among the 2987 participants, 2464 were classified as non-depressed at baseline. Of those, 718 developed incident depression (29.1%) during the 20 years of follow-up. The risk of incident depression was significantly reduced in board game players after adjustment on age, gender, education, marital status, history of stroke and diabetes (HR=0.84; 95%CI=0.72-0.98; p<0.03). This relationship remained almost unchanged but was only borderline significant after adjustment on MMSE score at baseline screening (HR=0.87; 95%CI=0.74-1.02; p=0.08).

Discussion

Playing board games is a common stimulating leisure activity in elderly French people since one third of subjects older than 65 in the general population reported regularly practising it. The rate of such activity remained high even in very old age and in subjects with cognitive deficit. Using the Paquid cohort data with 20 years of follow-up, which is one of the longest duration of follow-up in the world for a population-based cohort, we now show that board game players have a 15% lower risk of developing dementia than non-players. This reduced risk does not seem to be only a short-term effect as previously reported [9] but is also a long-term effect with a reduction observed one or even two decades after the baseline collection of this popular leisure activity. The association between board game playing and the risk of dementia remained robust after adjustment on confounding variables such as age, gender, educational level, marital status, and presence or absence of stroke or diabetes.

Our results are in accordance with findings from the Bronx Aging Cohort [10] conducted in a different population in the USA. However, in our study, the relationship disappeared after adjustment on baseline cognition and depression, which are known to be strong predictors of dementia. This means that the reduced risk of dementia could be related to the fact that board game players had better cognitive performances and were less depressed at baseline screening than non-players. On the contrary, baseline MMSE score and depression appeared to be significantly related to the subsequent risk of dementia.

To test whether cognitive decline and the occurrence of depression were mediating factors in the relationship between playing board games and dementia, we studied non-demented subjects with regard to the risk of cognitive decline and incident depression in board game players versus non-players. Board game players had significantly less cognitive decline and less incident depression than non-players. Thus, cognitive decline and depression

have the three statistical conditions to be considered as mediating factors [17]: cognitive decline and depression were associated with an increased risk of dementia; board game playing was associated with a reduced risk of cognitive decline and depression; and after multivariate analysis, playing board games was no longer significantly associated with dementia, unlike MMSE score and depression at baseline. This means that playing board games seems to have a favourable effect on cognition and depression before dementia and could therefore have a favourable effect on the risk of dementia. Another argument for a possible mediation is that cognitive decline and depressive symptoms are likely used to diagnose dementia. Of course, we cannot exclude that an unmeasured cognitive decline before baseline could precede the discontinuation of board game playing. The relationship could be bidirectional. Only repeated measures of board game playing along with repeated measures of depression and cognition could disentangle this relationship.

Several explanations could be given to explain the relationship between board game playing, cognitive decline, depression and then dementia. Less board game playing might be an early marker or an early consequence of dementia that precedes the decline in MMSE score and the occurrence of depression before dementia. The disappearance of the significant relationship after exclusion of incident demented cases occurring during the follow-up of the cohort is in favour of a reverse causation. However a decrease of statistical power and a selection of the sample could also explain these results. Another explanation could be that board game playing is a marker of behaviour that promotes successful aging, and that this could be the real non-specific factor protecting against cognitive decline, depression and then dementia [18]. If board game playing is only a marker of an ongoing subclinical process or of a specific personality, changing this activity would have no consequence on the risk of dementia.

Alternatively, board game playing might increase or preserve cognitive reserve, thereby delaying the clinical onset of dementia [1] or slowing the pathological process of the disease [10]. If this explanation was true, increase or promote this activity could contribute to decrease the risk of dementia in elderly people.

Because of the observational nature of our study, there is a possibility of residual or unmeasured confounding. For example, we did not adjust on all genetic factors, excepted on ApoE4 available only in a small number of the Paquid subjects. The observed association between board game playing and dementia appears to be independent from educational level and marital status, which may influence people's involvement in board game playing.

Our study has other limitations. Although standard criteria and well-established procedures were used to make the diagnoses, misclassification is inevitable. Only reported regular activities were collected at baseline without direct measurement, although the history was checked by informants whenever possible. We had no precise data on the frequency and duration of board game playing. It is reasonable to expect that board game playing may be endorsed once every 2 or 4 weeks, and that these board game players were considered in our analyses as non-players.

The refusal rate during the follow-up of the cohort was quite low, but many more subjects died than became demented. However, the risk of death was lower in players than in non-players. Even if a competitive risk between death and dementia might occur, it would lead to an underestimation of the risk of dementia in non-players.

Although this epidemiological study suggests that playing board games has a protective effect on cognitive decline, depression and then dementia, the evidence is not definitive. Only controlled studies could truly establish whether playing board games is beneficial and could rule out a reverse causation. However, such a trial appears almost impossible to organize without the possibility of blinding. Even if the evidence is not completely documented, the immediate pleasure procured by playing board games, the advantages that social interaction offers and the ease of applying such a measure in the real world without any drawbacks mean that this activity could be promoted for successful aging.

The present findings, which replicate those obtained with another cohort study in a different elderly population, suggest recommending board game playing in old age to reduce the risk of cognitive decline and depression, and in turn to reduce the risk of dementia.

Acknowledgments and Funding The Paquid study was founded by Novartis pharma, IPSEN pharma, Conseil Régional d'Aquitaine and Institute for European expertise in physiology

Competing interests No competing interests

Contributor statement

JFD was involved in the design, data collection, analysis, he advised on data interpretation and wrote the initial draft. AFS was involved in analysis and she advised on data interpretation. MLG was involved in data collection, analysis and she advised on data interpretation. MV advised on data interpretation. HA was involved in the design and data collection. JMO was involved in the design and data collection. PBG was involved in design and data collection. CH was involved in design, data collection, analysis and she advised on data interpretation. All authors read and approved the final manuscript.

Patient consent Obtained

Ethics approval Ethics approval was provided by the Bordeaux 2 University Ethics Committee in 1988.

Data Sharing JF Dartigues declare that the data for this article are available if required.

References

1. Stern, Y., *Cognitive reserve in ageing and Alzheimer's disease.* Lancet Neurol, 2012; **11**: 1006-12.
2. Akbaraly, T.N., et al., *Leisure activities and the risk of dementia in the elderly: results from the Three-City Study.* Neurology 2009; **73**:854-61.
3. Stern, Y., et al., *Space Fortress game training and executive control in older adults: a pilot intervention.* Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 2011;**18**:653-77.
4. Barnes, D.E., et al., *Computer-based cognitive training for mild cognitive impairment: results from a pilot randomized, controlled trial.* Alzheimer Dis Assoc Disord 2009;**23**:205-10.
5. Cohen, G.D., et al., *The first therapeutic game specifically designed and evaluated for Alzheimer's disease.* Am J Alzheimers Dis Other Demen 2008;**23**:540-51.
6. Bosch-Domenech, A., R. Nagel, and J.V. Sanchez-Andres, *Prosocial capabilities in Alzheimer's patients.* J Gerontol B Psychol Sci Soc Sci 2010;**65B**:119-28.
7. Clarkson-Smith, L. and A.A. Hartley, *The game of bridge as an exercise in working memory and reasoning.* J Gerontol 1990;**45**:233-8.
8. Nouchi, R., et al., *Brain training game improves executive functions and processing speed in the elderly: a randomized controlled trial.* PLoS One 2012;**7**:29676.
9. Fabrigoule, C., et al., *Social and leisure activities and risk of dementia: a prospective longitudinal study.* J Am Geriatr Soc 1995;**43**: 485-90.
10. Verghese, J., et al., *Leisure activities and the risk of dementia in the elderly.* N Engl J Med 2003; **348**:2508-16.
11. Hughes, T.F., et al., *Engagement in reading and hobbies and risk of incident dementia: the MoVIES project.* Am J Alzheimers Dis Other Demen 2010;**25**:432-8.
12. Dartigues, J.F., et al., *[The Paquid research program on the epidemiology of dementia. Methods and initial results].* Rev Neurol (Paris) 1991;**147**:225-30.
13. Folstein, M.F., S.E. Folstein, and P.R. McHugh, *"Mini-mental state". A practical method for grading the cognitive state of patients for the clinician.* J Psychiatr Res 1975;**12**:189-98.
14. Fuhrer, R., et al., *Depressive symptomatology and cognitive functioning: an epidemiological survey in an elderly community sample in France.* Psychol Med 1992;**22**:159-72.
15. Proust-Lima, C., J.F. Dartigues, and H. Jacqmin-Gadda, *Misuse of the linear mixed model when evaluating risk factors of cognitive decline.* Am J Epidemiol 2011;**174**:1077-88.
16. Amieva, H., et al., *Prodromal Alzheimer's disease: Successive emergence of the clinical symptoms.* Ann Neurol 2008;**64**:492-498.
17. Baron, R.M. and D.A. Kenny, *The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations.* J Pers Soc Psychol 1986;**51**:1173-82.
18. Dartigues, J.F. and C. Feart, *Risk factors for Alzheimer disease: aging beyond age?* Neurology 2011; **77**:206-7.

Figure 1. Probability of survival without dementia according to regular board game playing. Kaplan Meier Estimates.

Title : Playing board games, cognitive decline and dementia: a French population-based cohort study

Authors : Jean François Dartigues[1], Alexandra Foubert-Samier[1], Mélanie Le Goff[1], Mélanie Viltard[2], Hélène Amieva[1], Jean Marc Orgogozo[1], Pascale Barberger-Gateau[1], Catherine Helmer[1]

Adresses : 1 INSERM U 897, Université Bordeaux Ségalen, 146 rue Léo Saignat, 33076 Bordeaux cedex, France

2 IEEP, Institute for European expertise in physiology, 21, rue Leblanc 75015 Paris, France

Corresponding author : Jean François Dartigues, INSERM U 897, Université Bordeaux Ségalen, 146 rue Léo Saignat, 33076 Bordeaux cedex, France
Tel : +33 5 57571596 Fax : +33 5 57571486
Email : jfd@isped.u-bordeaux2.fr

Key words : Dementia, epidemiology, board games, risk factors, mediating factors

Word count : 2,846 words

Abstract

Objectives: To study the relationship between board game-playing and risk of subsequent dementia in the Paquid cohort.

Design: A prospective population-based study.

Setting: in the Bordeaux area in South Western France.

Participants: 3,675 non-demented subjects at baseline.

Primary outcome measure: the risk of dementia during the twenty years of follow-up.

Results: Among 3,675 non-demented subjects at baseline, 32.2% reported regular board game playing. Eight hundred and forty subjects developed dementia during the twenty years of follow-up. The risk of dementia was fifteen per cent lower in board game players than in non-players (Hazard Ratio =0.85; 95% Confidence Interval = 0.74-0.99; p=0.04) after adjustment on age, gender, education and other confounders. The statistical significance disappeared after supplementary adjustment on baseline MMSE and depression (HR=0. 96; 95% CI = 0.82-1.12; p=0.61). However, board game players had less decline in their MMSE score during the follow-up of the cohort (β=0.011, p=0.03) and less incident depression than non-players (HR=0.84; 95%CI=0.72-0.98; p<0.03).

Conclusions: A possible beneficial effect of board game-playing on the risk of dementia could be mediated by less cognitive decline and less depression in elderly board game players.

Article summery

Article focus:

- Stimulating leisure activities are considered as possible protective factors against dementia and cognitive decline in elderly people, particularly due to enhancement of cognitive reserve.
- Previous papers have shown that playing games can improve cognitive performances in healthy elderly subject, but controversial results were obtained in dementia. Thus, playing board games could be a particularly relevant way to preserve cognition and to prevent cognitive decline or dementia, and could be recommended without any real drawbacks provided the favourable relationship between playing games and dementia is confirmed.
- However, to our knowledge, few authors have studied the relationship between playing board games and the risk of subsequent dementia in prospective cohort studies.

Key messages:

- Using the Paquid cohort data with 20 years of follow-up, we now show that board game players have a 15% lower risk of developing dementia than non-players.
- This reduce risk does not seem to be only a short-term effect as previously reported but is also a long-term effect with a reduction observed one or even two decades after baseline collection of this popular leisure activity. However, in our study, the relationship disappeared after adjustment on baseline cognition and depression, which are known to be strong predictors of dementia.
- A possible beneficial effect of board game-playing on the risk of dementia could be mediated by less cognitive decline and less depression in elderly board game players.

Strengths and limitations:

- With 20 years of follow-up, the Paquid cohort study is one of the longest duration of follow-up in the world for a population-based cohort.
- Because of the observational nature of our study, there is a possibility of residual or unmeasured confounding such as genetic factors.
- Although standard criteria and well-established procedures were used to make the diagnoses, misclassification is inevitable. Only reported regular activities were collected at baseline without direct measurement, although the history was checked by

informants whenever possible. We had no precise data on the frequency and duration of board game playing.

Stimulating leisure activities are considered as possible protective factors against dementia and cognitive decline in elderly people, particularly due to enhancement of cognitive reserve [1-2]. Cognitive reserve is considered as one of the major explanations for differences between individuals in susceptibility to age-related brain changes and pathology related to Alzheimer's disease. Individuals with a large cognitive reserve can tolerate more of these changes than others and maintain their functions [1]. Playing board games is one of the most stimulating leisure activities for elderly people, even at an advanced age, and it has specific advantages compared to other games or activities. Playing board games is a recreational activity that promotes exposure to novelty, taking initiatives, planning, adaptation to winning or losing, and brings immediate pleasure to participants. In addition, playing games is an activity that can be undertaken with family members or friends and even with strangers, and it promotes social interaction and exchange with different generations. Furthermore, it is an inexpensive leisure activity that involves a wide range of tasks from simple ones as in bingo to complex ones as in bridge, and such games can be adapted to the level of the players. Finally, elderly people with physical disability, mild hearing or visual impairment can continue to participate in this stimulating leisure activity, irrespective of the season or the weather. Other stimulating leisure activities like reading, travelling, gardening, doing odd jobs or playing sports do not offer the same advantages and ease of practice. Thus, playing board games could be a particularly relevant way to preserve cognition and to prevent cognitive decline or dementia, and could be recommended without any real drawbacks provided the favourable relationship between playing games and dementia is confirmed.

Previous papers have shown that playing games can improve cognitive performances in healthy elderly subjects [3], but controversial results were obtained in mild cognitive impairment [4] or in dementia [5-6]. Playing games is known to enhance cognitive performances in working memory, executive function, semantic memory and logical reasoning [3, 7-8]. However, to our knowledge, few authors have studied the relationship between playing board games and the risk of subsequent dementia in prospective cohort studies.

In a previous paper on the Paquid population-based cohort, we found that playing board games was significantly associated with a reduced risk of incident dementia three years later [9]. However, the results were obtained after a short follow-up and the significance disappeared after adjustment on cognitive performances at baseline. Similar results were obtained after 20 years of follow-up by Verghese et al in the Bronx Aging Study [10]. On the

contrary, in the MoVIES project, Hughes et al [11] studying different types of games found that only doing crossword puzzles was associated with a reduced risk of dementia while other games like bridge, other card games and other board games were not. Thus, the relationship remains uncertain and more evidence is needed to support preventive recommendations to elderly people about playing board games.

With the prolonged follow-up of the Paquid study with repeated measures of cognition, depression and clinical dementia, we re-analysed the relationship between playing board games collected at the baseline screening of the participants and the occurrence of dementia during the 20 years of follow-up of the cohort. Moreover, we analysed whether depression and cognitive decline before dementia could mediate the relationship between playing board games and dementia.

Methods

Study population

The data came from the Paquid cohort, an epidemiological prospective study on cerebral and functional aging with over 20 years of follow-up. The methodology has been previously described [12]. In brief, the initial baseline sample included 3,777 community dwellers, aged 65 or more, randomly selected from the electoral rolls in 75 different sites of two French administrative districts (Departments of Gironde and Dordogne). The participants were representative of the elderly community dwellers of the area in terms of age and sex. Since the baseline visit in 1988, the participants have been revisited at home by a dedicated neuropsychologist up to nine times over the entire follow-up. After 22 years, the Paquid cohort is still ongoing. The present analyses were conducted on the data collected over a 20-year period of follow-up.

Data collection

Leisure and social activities were collected at baseline by a standardized questionnaire during a face-to-face interview conducted by a psychologist. Ten activities were explored with the question: “Do you usually undertake this activity (at least once a week): yes or no?” The following activities were screened: reading, gardening, doing odd jobs or knitting, watching television, participating in sports, playing board games, looking after children, participating in group activities or associations, visiting friends or family members and travelling. Only playing board games was considered in this paper. Board games comprised card games, bingo, chess, draughts and other parlour games.

A neuropsychological battery was conducted at baseline and at each follow-up visit with assessment of visual memory, verbal memory, language, executive function and simple logical reasoning [12]. A French version of the Mini-Mental State Examination (MMSE) [13] was used as an index of global cognitive performance. Scores range from 0 to 30. Depressive symptomatology was assessed at each follow-up screening using the French version of the Centre for Epidemiological Studies Depression Scale (CES-D) [14]. This is a 20-item self-report scale developed for use in epidemiological studies in the community. Scores range from 0 to 60 according to the frequency of the depressive symptoms during the previous week. According to a previous validation study for the French population, CES-D cut-off scores of 17 for men and 23 for women indicate clinically relevant depression [14]. Subjects were considered as having depression if they were treated by anti-depressors or had a score above the cut-off score at the CESD.

At baseline and at each follow-up visit, after the neuropsychological evaluation, the neuropsychologist filled in the Diagnostic and Statistical Manual of Mental Disorders 3rd ed. revised (DSM-IIIR) to identify subjects suspected of being demented. These cases and those with at least a three-point decline in MMSE score since the previous visit were examined at home by a neurologist to confirm or not the diagnosis of dementia and specify the etiology. All diagnoses of dementia were assigned at a case consensus conference attended by the study neurologist and two other dementia specialists according to the DSM-IIIR criteria. When evaluating cognitive status, the members of the consensus conference had no knowledge of leisure activities practiced by subjects.

Statistical analyses

Descriptive and comparative analyses were conducted using appropriate tests (*t*-test or chi-square test). Kaplan-Meier curves for the risk of incident dementia were obtained for the two categories of subjects according to their board game playing and compared with the Log Rank test.

To estimate the risk of dementia associated with game-playing, incident cases of dementia occurring between the baseline screening and the 20th year of follow-up were considered as an outcome variable. The time-to-event was defined as the time from baseline to the date of a diagnosis of dementia or to the last follow-up for subjects without dementia. Participants were censored at the time of diagnosis of dementia or at the last follow-up for those non-demented. Adjustment on possible confounders was performed with the multivariate Cox proportional hazards model with delayed entry taking age as time scale**.** The

multivariate model included the following covariates: gender, educational level (classified in five levels: high school, college, secondary level, primary school with diploma, primary school without diploma or no schooling), marital status, self-reported diabetes and stroke (model 1). Supplementary adjustment was made on self-reported visual, hearing impairment and ApoE 4 genotype on the subsample of the cohort with blood sampling (n=623).

We examined the influence of baseline cognitive performances on the MMSE score and the presence of depression at baseline (model 2). Risk of cognitive decline was analysed by a multivariate mixed model taking repeated values of the MMSE score during the 20 years of follow-up as outcome. Beta transformation of the MMSE score was used to take into account the ceiling effect of the test in non-demented cases [15]. Board game playing was considered as covariate with adjustment on confounders as in the previous multivariate model.

To estimate the risk of incident depression associated with board game-playing, incident cases of depression occurring between the baseline screening and the 20th year of follow-up were considered as the outcome variable. The time-to-event was defined as the time from baseline to the date of a diagnosis of depression or to the last follow-up for subjects without depression. Participants were censored at the time of the first diagnosis of depression during the follow-up or at the last follow-up for those never depressed over the follow-up. Adjustment on possible confounders was performed with the multivariate Cox proportional hazards model using the same adjustments as previously.

The analyses were performed using SAS, version 9.2 (SAS Institute, Inc., Cary, NC).

Results

Characteristics of board game players

Among the 3,777 participants, 102 (2.7%) were classified as prevalent cases of dementia at the baseline screening and excluded from the sample. Of the remaining 3675 subjects, five had missing data for board game playing (0.1%). One thousand one hundred and eighty-one subjects reported regular board game playing (32.2%). Board game players were younger, more educated, more often married, less depressed and had better cognitive performances at baseline screening than non-players (Table 1). However, the proportion of board game players remained high in very old age (18% in subjects aged from 85 to 89 years, and even 12.5% in those older than 89 years), and even in non-demented subjects with low cognitive performances (18.8% in subjects with an MMSE between 20 and 23, 10.6% in subjects with an MMSE lower than 20). In the subsample of 623 subjects with blood sampling

the proportion of ApoE 4 carriers was the same in both groups (23.5% for non-players vs 21.2 for players %, p=0.5).

Table 1. Characteristics of participants according to board game playing. Paquid Study n=3670

	Players (n=1181)	Non-players (n=2489)	p value
Gender (males)	501 (42.4)	1039 (41.7)	0.70
Age at inclusion (years): mean (SD)	73.6 (5.9)	76.0 (7.1)	<0.0001
Educational Level (higher)			
Primary school without diploma or no schooling	302 (25.6)	976 (39.2)	
Primary school with diploma	546 (46.2)	1058 (42.5)	
Secondary level	179 (15.2)	228 (9.2)	<0.0001
College	77 (6.5)	127 (5.1)	
High school	77 (6.5)	100 (4.0)	
Marital Status			0.0305
Married	708 (59.9)	1394 (56.0)	
Widowed	381 (32.3)	905 (36.4)	
Single	52 (4.4)	127 (5.1)	
Divorced	40 (3.4)	63 (2.5)	
Diabetes	87 (7.4)	219 (8.8)	0.14
Stroke	42 (3.6)	152 (6.1)	0.0012
MMSE score at inclusion: mean (SD)	26.9 (2.6)	25.3 (3.6)	<0.0001
Depression at inclusion	116 (9.9)	494 (20.4)	<0.0001
ApoE 4 genotype (carriers)*	48 (21.2)	93 (23.5)	0.5

Unless otherwise stated values are numbers (%)

SD: Standard Deviation

* n= 623 (396 non-players and 227 players)

Board game-playing and risk of incident dementia

Among the 3670 participants, 2987 (81.4%) were seen again at least once during the twenty years of follow-up. One hundred and forty-two persons deceased before the first screening (3.9%) and 541 refused to participate or were lost to follow-up (14.7%). The proportion of board game players was greater in those who were followed-up at least once.

Eight hundred and thirty cases of incident dementia (27.8%) were observed during the twenty years of follow-up. The cumulative risk of dementia was significantly reduced in subjects board game players versus non-players (Log rank test = 24.2, p<0.001). After three years of follow-up, 3% of board players developed dementia versus 6% of non-players, 16% versus 27% after ten years and 47% versus 58% after twenty years (Figure 1).

After adjustment on age, gender, education, marital status, history of stroke and diabetes (Table 2), the risk of dementia remained significantly reduced (HR = 0.85, 95%CI= 0.74-0.99, p=0.04). The relationship remained unchanged after supplementary adjustment on visual and hearing impairment. However, the relationship was no longer significant after supplementary adjustment on depression and MMSE score at baseline (HR=0.96, 95%CI=0.82-1.12, p=0.61). In the latter model, depression (HR=1.34, 95%CI=1.12-1.60, p=0.0011) and MMSE score at baseline (for one point fewer HR=1.10, 95%CI=1.08-1.12, p<0.0001) were strong predictors of dementia. In supplementary analyses, we found that after separated adjustment on MMSE and depression, the significant relationships between board game playing and dementia disappeared in both analyses, but most of the effect seems to be due to controlling for MMSE.

Finally, we made a supplementary adjustment on ApoE 4 genotype on a subsample of the Paquid cohort of 618 subjects. In this subsample of subjects, after adjustment on ApoE 4 genotype (carriers vs no carriers), the HR for dementia related to playing board game decreased to 0.74 but was no more significant (p=0.06).

Table 2. Risk of dementia according to board game playing in the Paquid cohort. Multivariate Cox model.

	Model 1*			Model 2**		
	HR	95%CI	p Value	HR	95%CI	p Value
Board game (players vs non-players)	0.85	0.74-0.99	0.04	0.96	0.82-1.13	0.62
Gender (female vs male)	1.29	1.10-1.52	0.002	1.23	1.04-1.46	0.01
Education (higher vs lower)						
Primary school with diploma	0.65	0.56-0.76	<0.0001	0.85	0.72-1.01	0.07
Secondary level	0.58	0.45-0.74	<0.0001	0.84	0.64-1.11	0.22
College	0.50	0.36-0.71	0.0001	0.76	0.53-1.09	0.13
High school	0.38	0.25-0.58	<0.0001	0.57	0.37-0.88	0.01
marital status						
widowed vs married	0.89	0.76-1.05	0.16	0.85	0.72-1.00	0.05
single vs married	1.28	0.93-1.75	0.12	1.20	0.86-1.68	0.28
divorced vs married	1.16	0.77-1.74	0.49	1.06	0.70-1.61	0.78
history of stroke (yes vs no)	1.55	1.17-2.05	0.0016	1.31	0.97-1.78	0.08
Diabetes (yes vs no)	1.10	0.84-1.46	0.48	1.05	0.79-1.40	0.72
MMSE score				0.91	0.89-0.93	<0.0001
Depression (yes vs no)				1.34	1.12-1.59	0.001

* Adjustment on age, gender, education, marital status, history of stroke and diabetes

** Adjustment on age, gender, education, marital status, history of stroke, diabetes, MMSE score and depression

Board game-playing, cognitive decline and risk of incident depression

Board game players had less cognitive decline in MMSE score than non-players after adjustment on age, gender, education, marital status, history of stroke and diabetes (β=0.011, p=0.03). The relationship remained unchanged after supplementary adjustment on depression at baseline (β=0.010, p=0.04). The cognitive decline may begin several years before the diagnosis of dementia as showed by us [16]. To explore a possible reverse causation, we studied the relationship between board game playing and the cognitive decline, eliminating those who became demented over the first 10 years of follow-up and over the entire period.

The beta coefficients slightly decrease (from 0.01 to 0.008) but become non significant (respectively p=0.07 and p=0.15).

Among the 2987 participants, 2464 were classified as non-depressed at baseline. Of those, 718 developed incident depression (29.1%) during the 20 years of follow-up. The risk of incident depression was significantly reduced in board game players after adjustment on age, gender, education, marital status, history of stroke and diabetes (HR=0.84; 95%CI=0.72-0.98; p<0.03). This relationship remained almost unchanged but was only borderline significant after adjustment on MMSE score at baseline screening (HR=0.87; 95%CI=0.74-1.02; p=0.08).

Discussion

Playing board games is a common stimulating leisure activity in elderly French people since one third of subjects older than 65 in the general population reported regularly practising it. The rate of such activity remained high even in very old age and in subjects with cognitive deficit. Using the Paquid cohort data with 20 years of follow-up, which is one of the longest duration of follow-up in the world for a population-based cohort, we now show that board game players have a 15% lower risk of developing dementia than non-players. This reduced risk does not seem to be only a short-term effect as previously reported [9] but is also a long-term effect with a reduction observed one or even two decades after the baseline collection of this popular leisure activity. The association between board game playing and the risk of dementia remained robust after adjustment on confounding variables such as age, gender, educational level, marital status, and presence or absence of stroke or diabetes.

Our results are in accordance with findings from the Bronx Aging Cohort [10] conducted in a different population in the USA. However, in our study, the relationship disappeared after adjustment on baseline cognition and depression, which are known to be strong predictors of dementia. This means that the reduced risk of dementia could be related to the fact that board game players had better cognitive performances and were less depressed at baseline screening than non-players. On the contrary, baseline MMSE score and depression appeared to be significantly related to the subsequent risk of dementia.

To test whether cognitive decline and the occurrence of depression were mediating factors in the relationship between playing board games and dementia, we studied non-demented subjects with regard to the risk of cognitive decline and incident depression in board game players versus non-players. Board game players had significantly less cognitive decline and less incident depression than non-players. Thus, cognitive decline and depression

have the three statistical conditions to be considered as mediating factors [17]: cognitive decline and depression were associated with an increased risk of dementia; board game playing was associated with a reduced risk of cognitive decline and depression; and after multivariate analysis, playing board games was no longer significantly associated with dementia, unlike MMSE score and depression at baseline. This means that playing board games seems to have a favourable effect on cognition and depression before dementia and could therefore have a favourable effect on the risk of dementia. Another argument for a possible mediation is that cognitive decline and depressive symptoms are likely used to diagnose dementia. Of course, we cannot exclude that an unmeasured cognitive decline before baseline could precede the discontinuation of board game playing. The relationship could be bidirectional. Only repeated measures of board game playing along with repeated measures of depression and cognition could disentangle this relationship.

Several explanations could be given to explain the relationship between board game playing, cognitive decline, depression and then dementia. Less board game playing might be an early marker or an early consequence of dementia that precedes the decline in MMSE score and the occurrence of depression before dementia. The disappearance of the significant relationship after exclusion of incident demented cases occurring during the follow-up of the cohort is in favour of a reverse causation. However a decrease of statistical power and a selection of the sample could also explain these results. Another explanation could be that board game playing is a marker of behaviour that promotes successful aging, and that this could be the real non-specific factor protecting against cognitive decline, depression and then dementia [18]. If board game playing is only a marker of an ongoing subclinical process or of a specific personality, changing this activity would have no consequence on the risk of dementia.

Alternatively, board game playing might increase or preserve cognitive reserve, thereby delaying the clinical onset of dementia [1] or slowing the pathological process of the disease [10]. If this explanation was true, increase or promote this activity could contribute to decrease the risk of dementia in elderly people.

Because of the observational nature of our study, there is a possibility of residual or unmeasured confounding. For example, we did not adjust on all genetic factors, excepted on ApoE4 available only in a small number of the Paquid subjects. The observed association between board game playing and dementia appears to be independent from educational level and marital status, which may influence people's involvement in board game playing.

Our study has other limitations. Although standard criteria and well-established procedures were used to make the diagnoses, misclassification is inevitable. Only reported regular activities were collected at baseline without direct measurement, although the history was checked by informants whenever possible. We had no precise data on the frequency and duration of board game playing. It is reasonable to expect that board game playing may be endorsed once every 2 or 4 weeks, and that these board game players were considered in our analyses as non-players.

The refusal rate during the follow-up of the cohort was quite low, but many more subjects died than became demented. However, the risk of death was lower in players than in non-players. Even if a competitive risk between death and dementia might occur, it would lead to an underestimation of the risk of dementia in non-players.

Although this epidemiological study suggests that playing board games has a protective effect on cognitive decline, depression and then dementia, the evidence is not definitive. Only controlled studies could truly establish whether playing board games is beneficial and could rule out a reverse causation. However, such a trial appears almost impossible to organize without the possibility of blinding. Even if the evidence is not completely documented, the immediate pleasure procured by playing board games, the advantages that social interaction offers and the ease of applying such a measure in the real world without any drawbacks mean that this activity could be promoted for successful aging.

The present findings, which replicate those obtained with another cohort study in a different elderly population, suggest recommending board game playing in old age to reduce the risk of cognitive decline and depression, and in turn to reduce the risk of dementia.

Acknowledgments and Funding The Paquid study was founded by Novartis pharma, IPSEN pharma, Conseil Régional d'Aquitaine and Institute for European expertise in physiology

Competing interests No competing interests

Contributor statement

JFD was involved in the design, data collection, analysis, he advised on data interpretation and wrote the initial draft. AFS was involved in analysis and she advised on data interpretation. MLG was involved in data collection, analysis and she advised on data interpretation. MV advised on data interpretation. HA was involved in the design and data collection. JMO was involved in the design and data collection. PBG was involved in design and data collection. CH was involved in design, data collection, analysis and she advised on data interpretation. All authors read and approved the final manuscript.

Patient consent Obtained

Ethics approval Ethics approval was provided by the Bordeaux 2 University Ethics Committee in 1988.

Data Sharing JF Dartigues declare that the data for this article are available if required.

References

1. Stern, Y., *Cognitive reserve in ageing and Alzheimer's disease.* Lancet Neurol, 2012; **11**: 1006-12.
2. Akbaraly, T.N., et al., *Leisure activities and the risk of dementia in the elderly: results from the Three-City Study.* Neurology 2009; **73**:854-61.
3. Stern, Y., et al., *Space Fortress game training and executive control in older adults: a pilot intervention.* Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 2011;**18**:653-77.
4. Barnes, D.E., et al., *Computer-based cognitive training for mild cognitive impairment: results from a pilot randomized, controlled trial.* Alzheimer Dis Assoc Disord 2009;**23**:205-10.
5. Cohen, G.D., et al., *The first therapeutic game specifically designed and evaluated for Alzheimer's disease.* Am J Alzheimers Dis Other Demen 2008;**23**:540-51.
6. Bosch-Domenech, A., R. Nagel, and J.V. Sanchez-Andres, *Prosocial capabilities in Alzheimer's patients.* J Gerontol B Psychol Sci Soc Sci 2010;**65B**:119-28.
7. Clarkson-Smith, L. and A.A. Hartley, *The game of bridge as an exercise in working memory and reasoning.* J Gerontol 1990;**45**:233-8.
8. Nouchi, R., et al., *Brain training game improves executive functions and processing speed in the elderly: a randomized controlled trial.* PLoS One 2012;**7**:29676.
9. Fabrigoule, C., et al., *Social and leisure activities and risk of dementia: a prospective longitudinal study.* J Am Geriatr Soc 1995;**43**: 485-90.
10. Verghese, J., et al., *Leisure activities and the risk of dementia in the elderly.* N Engl J Med 2003; **348**:2508-16.
11. Hughes, T.F., et al., *Engagement in reading and hobbies and risk of incident dementia: the MoVIES project.* Am J Alzheimers Dis Other Demen 2010;**25**:432-8.
12. Dartigues, J.F., et al., *[The Paquid research program on the epidemiology of dementia. Methods and initial results].* Rev Neurol (Paris) 1991;**147**:225-30.
13. Folstein, M.F., S.E. Folstein, and P.R. McHugh, *"Mini-mental state". A practical method for grading the cognitive state of patients for the clinician.* J Psychiatr Res 1975;**12**:189-98.
14. Fuhrer, R., et al., *Depressive symptomatology and cognitive functioning: an epidemiological survey in an elderly community sample in France.* Psychol Med 1992;**22**:159-72.
15. Proust-Lima, C., J.F. Dartigues, and H. Jacqmin-Gadda, *Misuse of the linear mixed model when evaluating risk factors of cognitive decline.* Am J Epidemiol 2011;**174**:1077-88.
16. Amieva, H., et al., *Prodromal Alzheimer's disease: Successive emergence of the clinical symptoms.* Ann Neurol 2008;**64**:492-498.
17. Baron, R.M. and D.A. Kenny, *The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations.* J Pers Soc Psychol 1986;**51**:1173-82.
18. Dartigues, J.F. and C. Feart, *Risk factors for Alzheimer disease: aging beyond age?* Neurology 2011; **77**:206-7.

Figure 1. Probability of survival without dementia according to regular board game playing. Kaplan Meier Estimates.

STROBE Statement—checklist of items that should be included in reports of observational studies

Please fill out the page numbers on this form and upload the file as a supplemental file when you submit your revision

Manuscript Number_____

	Item No	Recommendation	Indicate page number ↓ (Or n/a if not applicable)
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	5-6
		(*c*) Explain how missing data were addressed	NA
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6-7
		(b) Indicate number of participants with missing data for each variable of interest	6
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	7
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA
		Cross-sectional study—Report numbers of outcome events or summary measures	NA
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95%	8-9

		confidence interval). Make clear which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

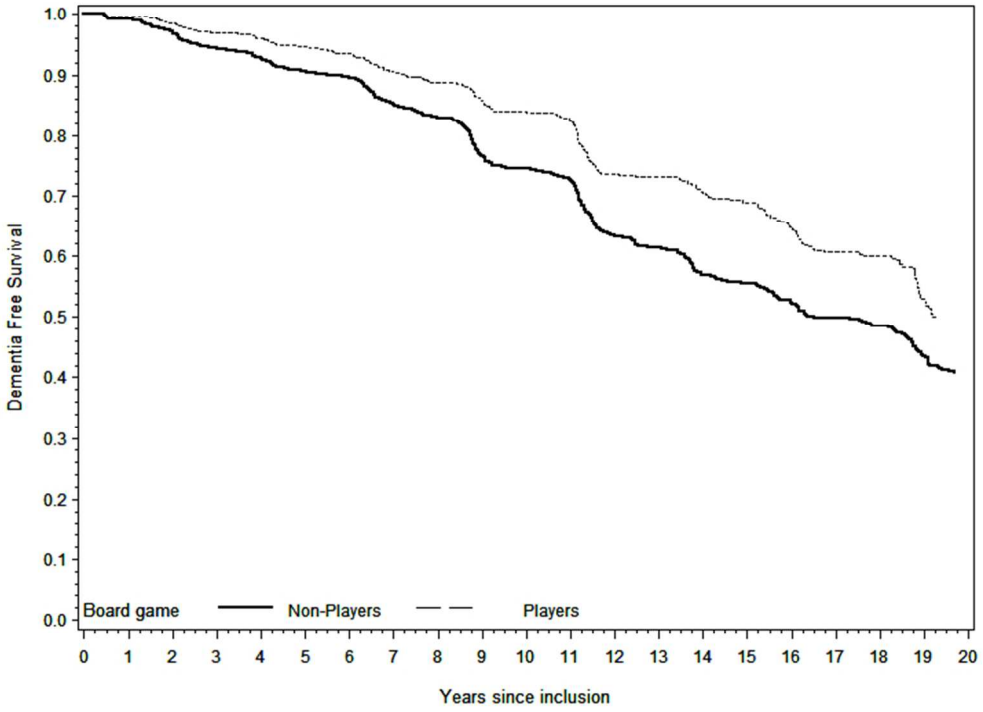

Figure 1. Probability of survival without dementia according to regular board game playing. Kaplan Meier Estimates.
184x151mm (100 x 100 DPI)

BMJ open

Playing board games, cognitive decline and dementia: a French population-based cohort study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-002998.R2
Article Type:	Research
Date Submitted by the Author:	26-Jul-2013
Complete List of Authors:	Dartigues, Jean-Fran&#65533;ois; University of Bordeaux, Foubert, Alexandra; INSERM U 897, Epidemiology Le Goff, Mélanie; INSERM U 897, Epidemiology Viltard, Mélanie; Intitut for european expertise in Physiology, Amieva, Hélène; INSERM U 897, Epidemiology Orgogozo, Jean; INSERM U 897, Epidemiology Barberger-Gateau, Pascale; INSERM U 897, Epidemiology Helmer, Catherine; INSERM U 897, Epidemiology
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Neurology
Keywords:	Dementia < NEUROLOGY, Epidemiology , PUBLIC HEALTH

Title : Playing board games, cognitive decline and dementia: a French population-based cohort study

Authors : Jean François Dartigues[1], Alexandra Foubert-Samier[1], Mélanie Le Goff[1], Mélanie Viltard[2], Hélène Amieva[1], Jean Marc Orgogozo[1], Pascale Barberger-Gateau[1], Catherine Helmer[1]

Adresses : 1 INSERM U 897, Université Bordeaux Ségalen, 146 rue Léo Saignat, 33076 Bordeaux cedex, France

2 IEEP, Institute for European expertise in physiology, 21, rue Leblanc 75015 Paris, France

Corresponding author : Jean François Dartigues, INSERM U 897, Université Bordeaux Ségalen, 146 rue Léo Saignat, 33076 Bordeaux cedex, France
Tel : +33 5 57571596 Fax : +33 5 57571486
Email : jfd@isped.u-bordeaux2.fr

Key words : Dementia, epidemiology, board games, risk factors, mediating factors

Word count : 2,846 words

Abstract

Objectives: To study the relationship between board game-playing and risk of subsequent dementia in the Paquid cohort.

Design: A prospective population-based study.

Setting: in the Bordeaux area in South Western France.

Participants: 3,675 non-demented subjects at baseline.

Primary outcome measure: the risk of dementia during the twenty years of follow-up.

Results: Among 3,675 non-demented subjects at baseline, 32.2% reported regular board game playing. Eight hundred and forty subjects developed dementia during the twenty years of follow-up. The risk of dementia was fifteen per cent lower in board game players than in non-players (Hazard Ratio =0.85; 95% Confidence Interval = 0.74-0.99; p=0.04) after adjustment on age, gender, education and other confounders. The statistical significance disappeared after supplementary adjustment on baseline MMSE and depression (HR=0. 96; 95% CI = 0.82-1.12; p=0.61). However, board game players had less decline in their MMSE score during the follow-up of the cohort (β=0.011, p=0.03) and less incident depression than non-players (HR=0.84; 95%CI=0.72-0.98; p<0.03).

Conclusions: A possible beneficial effect of board game-playing on the risk of dementia could be mediated by less cognitive decline and less depression in elderly board game players.

Article summery

Article focus:

- Stimulating leisure activities are considered as possible protective factors against dementia and cognitive decline in elderly people, particularly due to enhancement of cognitive reserve.
- Previous papers have shown that playing games can improve cognitive performances in healthy elderly subject, but controversial results were obtained in dementia. Thus, playing board games could be a particularly relevant way to preserve cognition and to prevent cognitive decline or dementia, and could be recommended without any real drawbacks provided the favourable relationship between playing games and dementia is confirmed.
- However, to our knowledge, few authors have studied the relationship between playing board games and the risk of subsequent dementia in prospective cohort studies.

Key messages:

- Using the Paquid cohort data with 20 years of follow-up, we now show that board game players have a 15% lower risk of developing dementia than non-players.
- This reduce risk does not seem to be only a short-term effect as previously reported but is also a long-term effect with a reduction observed one or even two decades after baseline collection of this popular leisure activity. However, in our study, the relationship disappeared after adjustment on baseline cognition and depression, which are known to be strong predictors of dementia.
- A possible beneficial effect of board game-playing on the risk of dementia could be mediated by less cognitive decline and less depression in elderly board game players.

Strengths and limitations:

- With 20 years of follow-up, the Paquid cohort study is one of the longest duration of follow-up in the world for a population-based cohort.
- Because of the observational nature of our study, there is a possibility of residual or unmeasured confounding such as genetic factors.
- Although standard criteria and well-established procedures were used to make the diagnoses, misclassification is inevitable. Only reported regular activities were collected at baseline without direct measurement, although the history was checked by

informants whenever possible. We had no precise data on the frequency and duration of board game playing.

Stimulating leisure activities are considered as possible protective factors against dementia and cognitive decline in elderly people, particularly due to enhancement of cognitive reserve [1-2]. Cognitive reserve is considered as one of the major explanations for differences between individuals in susceptibility to age-related brain changes and pathology related to Alzheimer's disease. Individuals with a large cognitive reserve can tolerate more of these changes than others and maintain their functions [1]. Playing board games is one of the most stimulating leisure activities for elderly people, even at an advanced age, and it has specific advantages compared to other games or activities. Playing board games is a recreational activity that promotes exposure to novelty, taking initiatives, planning, adaptation to winning or losing, and brings immediate pleasure to participants. In addition, playing games is an activity that can be undertaken with family members or friends and even with strangers, and it promotes social interaction and exchange with different generations. Furthermore, it is an inexpensive leisure activity that involves a wide range of tasks from simple ones as in bingo to complex ones as in bridge, and such games can be adapted to the level of the players. Finally, elderly people with physical disability, mild hearing or visual impairment can continue to participate in this stimulating leisure activity, irrespective of the season or the weather. Other stimulating leisure activities like reading, travelling, gardening, doing odd jobs or playing sports do not offer the same advantages and ease of practice. Thus, playing board games could be a particularly relevant way to preserve cognition and to prevent cognitive decline or dementia, and could be recommended without any real drawbacks provided the favourable relationship between playing games and dementia is confirmed.

Previous papers have shown that playing games can improve cognitive performances in healthy elderly subjects [3], but controversial results were obtained in mild cognitive impairment [4] or in dementia [5-6]. Playing games is known to enhance cognitive performances in working memory, executive function, semantic memory and logical reasoning [3, 7-8]. However, to our knowledge, few authors have studied the relationship between playing board games and the risk of subsequent dementia in prospective cohort studies.

In a previous paper on the Paquid population-based cohort, we found that playing board games was significantly associated with a reduced risk of incident dementia three years later [9]. However, the results were obtained after a short follow-up and the significance disappeared after adjustment on cognitive performances at baseline. Similar results were obtained after 20 years of follow-up by Verghese et al in the Bronx Aging Study [10]. On the

contrary, in the MoVIES project, Hughes et al [11] studying different types of games found that only doing crossword puzzles was associated with a reduced risk of dementia while other games like bridge, other card games and other board games were not. Thus, the relationship remains uncertain and more evidence is needed to support preventive recommendations to elderly people about playing board games.

With the prolonged follow-up of the Paquid study with repeated measures of cognition, depression and clinical dementia, we re-analysed the relationship between playing board games collected at the baseline screening of the participants and the occurrence of dementia during the 20 years of follow-up of the cohort. Moreover, we analysed whether depression and cognitive decline before dementia could mediate the relationship between playing board games and dementia.

Methods

Study population

The data came from the Paquid cohort, an epidemiological prospective study on cerebral and functional aging with over 20 years of follow-up. The methodology has been previously described [12]. In brief, the initial baseline sample included 3,777 community dwellers, aged 65 or more, randomly selected from the electoral rolls in 75 different sites of two French administrative districts (Departments of Gironde and Dordogne). The participants were representative of the elderly community dwellers of the area in terms of age and sex. Since the baseline visit in 1988, the participants have been revisited at home by a dedicated neuropsychologist up to nine times over the entire follow-up. After 22 years, the Paquid cohort is still ongoing. The present analyses were conducted on the data collected over a 20-year period of follow-up.

Data collection

Leisure and social activities were collected at baseline by a standardized questionnaire during a face-to-face interview conducted by a psychologist. Ten activities were explored with the question: “Do you usually undertake this activity (at least once a week): yes or no?” The following activities were screened: reading, gardening, doing odd jobs or knitting, watching television, participating in sports, playing board games, looking after children, participating in group activities or associations, visiting friends or family members and travelling. Only playing board games was considered in this paper. Board games comprised card games, bingo, chess, draughts and other parlour games.

A neuropsychological battery was conducted at baseline and at each follow-up visit with assessment of visual memory, verbal memory, language, executive function and simple logical reasoning [12]. A French version of the Mini-Mental State Examination (MMSE) [13] was used as an index of global cognitive performance. Scores range from 0 to 30. Depressive symptomatology was assessed at each follow-up screening using the French version of the Centre for Epidemiological Studies Depression Scale (CES-D) [14]. This is a 20-item self-report scale developed for use in epidemiological studies in the community. Scores range from 0 to 60 according to the frequency of the depressive symptoms during the previous week. According to a previous validation study for the French population, CES-D cut-off scores of 17 for men and 23 for women indicate clinically relevant depression [14]. Subjects were considered as having depression if they were treated by anti-depressors or had a score above the cut-off score at the CESD.

At baseline and at each follow-up visit, after the neuropsychological evaluation, the neuropsychologist filled in the Diagnostic and Statistical Manual of Mental Disorders 3rd ed. revised (DSM-IIIR) to identify subjects suspected of being demented. These cases and those with at least a three-point decline in MMSE score since the previous visit were examined at home by a neurologist to confirm or not the diagnosis of dementia and specify the etiology. All diagnoses of dementia were assigned at a case consensus conference attended by the study neurologist and two other dementia specialists according to the DSM-IIIR criteria. When evaluating cognitive status, the members of the consensus conference had no knowledge of leisure activities practiced by subjects.

Statistical analyses

Descriptive and comparative analyses were conducted using appropriate tests (*t*-test or chi-square test). Kaplan-Meier curves for the risk of incident dementia were obtained for the two categories of subjects according to their board game playing and compared with the Log Rank test.

To estimate the risk of dementia associated with game-playing, incident cases of dementia occurring between the baseline screening and the 20th year of follow-up were considered as an outcome variable. The time-to-event was defined as the time from baseline to the date of a diagnosis of dementia or to the last follow-up for subjects without dementia. Participants were censored at the time of diagnosis of dementia or at the last follow-up for those non-demented. Adjustment on possible confounders was performed with the multivariate Cox proportional hazards model with delayed entry taking age as time scale**.** The

multivariate model included the following covariates: gender, educational level (classified in five levels: high school, college, secondary level, primary school with diploma, primary school without diploma or no schooling), marital status, self-reported diabetes and stroke (model 1). Supplementary adjustment was made on self-reported visual, hearing impairment and ApoE 4 genotype on the subsample of the cohort with blood sampling (n=623).

We examined the influence of baseline cognitive performances on the MMSE score and the presence of depression at baseline (model 2). Risk of cognitive decline was analysed by a multivariate mixed model taking repeated values of the MMSE score during the 20 years of follow-up as outcome. Beta transformation of the MMSE score was used to take into account the ceiling effect of the test in non-demented cases [15]. Board game playing was considered as covariate with adjustment on confounders as in the previous multivariate model.

To estimate the risk of incident depression associated with board game-playing, incident cases of depression occurring between the baseline screening and the 20th year of follow-up were considered as the outcome variable. The time-to-event was defined as the time from baseline to the date of a diagnosis of depression or to the last follow-up for subjects without depression. Participants were censored at the time of the first diagnosis of depression during the follow-up or at the last follow-up for those never depressed over the follow-up. Adjustment on possible confounders was performed with the multivariate Cox proportional hazards model using the same adjustments as previously**.**

The analyses were performed using SAS, version 9.2 (SAS Institute, Inc., Cary, NC).

Results

Characteristics of board game players

Among the 3,777 participants, 102 (2.7%) were classified as prevalent cases of dementia at the baseline screening and excluded from the sample. Of the remaining 3675 subjects, five had missing data for board game playing (0.1%). One thousand one hundred and eighty-one subjects reported regular board game playing (32.2%). Board game players were younger, more educated, more often married, less depressed and had better cognitive performances at baseline screening than non-players (Table 1). However, the proportion of board game players remained high in very old age (18% in subjects aged from 85 to 89 years, and even 12.5% in those older than 89 years), and even in non-demented subjects with low cognitive performances (18.8% in subjects with an MMSE between 20 and 23, 10.6% in subjects with an MMSE lower than 20). In the subsample of 623 subjects with blood sampling

the proportion of ApoE 4 carriers was the same in both groups (23.5% for non-players vs 21.2 for players %, p=0.5).

Table 1. Characteristics of participants according to board game playing. Paquid Study n=3670

	Players (n=1181)	Non-players (n=2489)	p value
Gender (males)	501 (42.4)	1039 (41.7)	0.70
Age at inclusion (years): mean (SD)	73.6 (5.9)	76.0 (7.1)	<0.0001
Educational Level (higher)			
Primary school without diploma or no schooling	302 (25.6)	976 (39.2)	
Primary school with diploma	546 (46.2)	1058 (42.5)	
Secondary level	179 (15.2)	228 (9.2)	<0.0001
College	77 (6.5)	127 (5.1)	
High school	77 (6.5)	100 (4.0)	
Marital Status			0.0305
Married	708 (59.9)	1394 (56.0)	
Widowed	381 (32.3)	905 (36.4)	
Single	52 (4.4)	127 (5.1)	
Divorced	40 (3.4)	63 (2.5)	
Diabetes	87 (7.4)	219 (8.8)	0.14
Stroke	42 (3.6)	152 (6.1)	0.0012
MMSE score at inclusion: mean (SD)	26.9 (2.6)	25.3 (3.6)	<0.0001
Depression at inclusion	116 (9.9)	494 (20.4)	<0.0001
ApoE 4 genotype (carriers)*	48 (21.2)	93 (23.5)	0.5

Unless otherwise stated values are numbers (%)

SD: Standard Deviation

* n= 623 (396 non-players and 227 players)

Board game-playing and risk of incident dementia

Among the 3670 participants, 2987 (81.4%) were seen again at least once during the twenty years of follow-up. One hundred and forty-two persons deceased before the first screening (3.9%) and 541 refused to participate or were lost to follow-up (14.7%). The proportion of board game players was greater in those who were followed-up at least once.

Eight hundred and thirty cases of incident dementia (27.8%) were observed during the twenty years of follow-up. The cumulative risk of dementia was significantly reduced in subjects board game players versus non-players (Log rank test = 24.2, $p<0.001$). After three years of follow-up, 3% of board players developed dementia versus 6% of non-players, 16% versus 27% after ten years and 47% versus 58% after twenty years (Figure 1).

After adjustment on age, gender, education, marital status, history of stroke and diabetes (Table 2), the risk of dementia remained significantly reduced (HR = 0.85, 95%CI= 0.74-0.99, p=0.04). The relationship remained unchanged after supplementary adjustment on visual and hearing impairment. However, the relationship was no longer significant after supplementary adjustment on depression and MMSE score at baseline (HR=0.96, 95%CI=0.82-1.12, p=0.61). In the latter model, depression (HR=1.34, 95%CI=1.12-1.60, p=0.0011) and MMSE score at baseline (for one point fewer HR=1.10, 95%CI=1.08-1.12, $p<0.0001$) were strong predictors of dementia. In supplementary analyses, we found that after separated adjustment on MMSE and depression, the significant relationships between board game playing and dementia disappeared in both analyses, but most of the effect seems to be due to controlling for MMSE.

Finally, we made a supplementary adjustment on ApoE 4 genotype on a subsample of the Paquid cohort of 618 subjects. In this subsample of subjects, after adjustment on ApoE 4 genotype (carriers vs no carriers), the HR for dementia related to playing board game decreased to 0.74 but was no more significant (p=0.06).

Table 2. Risk of dementia according to board game playing in the Paquid cohort. Multivariate Cox model.

	Model 1*			Model 2**		
	HR	95%CI	p Value	HR	95%CI	p Value
Board game (players vs non-players)	0.85	0.74-0.99	0.04	0.96	0.82-1.13	0.62
Gender (female vs male)	1.29	1.10-1.52	0.002	1.23	1.04-1.46	0.01
Education (higher vs lower)						
Primary school with diploma	0.65	0.56-0.76	<0.0001	0.85	0.72-1.01	0.07
Secondary level	0.58	0.45-0.74	<0.0001	0.84	0.64-1.11	0.22
College	0.50	0.36-0.71	0.0001	0.76	0.53-1.09	0.13
High school	0.38	0.25-0.58	<0.0001	0.57	0.37-0.88	0.01
marital status						
widowed vs married	0.89	0.76-1.05	0.16	0.85	0.72-1.00	0.05
single vs married	1.28	0.93-1.75	0.12	1.20	0.86-1.68	0.28
divorced vs married	1.16	0.77-1.74	0.49	1.06	0.70-1.61	0.78
history of stroke (yes vs no)	1.55	1.17-2.05	0.0016	1.31	0.97-1.78	0.08
Diabetes (yes vs no)	1.10	0.84-1.46	0.48	1.05	0.79-1.40	0.72
MMSE score				0.91	0.89-0.93	<0.0001
Depression (yes vs no)				1.34	1.12-1.59	0.001

* Adjustment on age, gender, education, marital status, history of stroke and diabetes

** Adjustment on age, gender, education, marital status, history of stroke, diabetes, MMSE score and depression

Board game-playing, cognitive decline and risk of incident depression

Board game players had less cognitive decline in MMSE score than non-players after adjustment on age, gender, education, marital status, history of stroke and diabetes (β=0.011, p=0.03). The relationship remained unchanged after supplementary adjustment on depression at baseline (β=0.010, p=0.04). The cognitive decline may begin several years before the diagnosis of dementia as showed by us [16]. To explore a possible reverse causation, we studied the relationship between board game playing and the cognitive decline, eliminating those who became demented over the first 10 years of follow-up and over the entire period. The beta coefficients slightly decrease (from 0.01 to 0.008) but become non significant

(respectively p=0.07 and p=0.15). However a decrease of statistical power and a selection of the sample could explain these results. At the whole, this supplementary analysis is more in favour of a reverse causation from outcome to exposure.

Among the 2987 participants, 2464 were classified as non-depressed at baseline. Of those, 718 developed incident depression (29.1%) during the 20 years of follow-up. The risk of incident depression was significantly reduced in board game players after adjustment on age, gender, education, marital status, history of stroke and diabetes (HR=0.84; 95%CI=0.72-0.98; p<0.03). This relationship remained almost unchanged but was only borderline significant after adjustment on MMSE score at baseline screening (HR=0.87; 95%CI=0.74-1.02; p=0.08).

Discussion

Playing board games is a common stimulating leisure activity in elderly French people since one third of subjects older than 65 in the general population reported regularly practising it. The rate of such activity remained high even in very old age and in subjects with cognitive deficit. Using the Paquid cohort data with 20 years of follow-up, which is one of the longest duration of follow-up in the world for a population-based cohort, we now show that board game players have a 15% lower risk of developing dementia than non-players. This reduced risk does not seem to be only a short-term effect as previously reported [9] but is also a long-term effect with a reduction observed one or even two decades after the baseline collection of this popular leisure activity. The association between board game playing and the risk of dementia remained robust after adjustment on confounding variables such as age, gender, educational level, marital status, and presence or absence of stroke or diabetes.

Our results are in accordance with findings from the Bronx Aging Cohort [10] conducted in a different population in the USA. However, in our study, the relationship disappeared after adjustment on baseline cognition and depression, which are known to be strong predictors of dementia. This means that the reduced risk of dementia could be related to the fact that board game players had better cognitive performances and were less depressed at baseline screening than non-players. On the contrary, baseline MMSE score and depression appeared to be significantly related to the subsequent risk of dementia.

To test whether cognitive decline and the occurrence of depression were mediating factors in the relationship between playing board games and dementia, we studied non-demented subjects with regard to the risk of cognitive decline and incident depression in board game players versus non-players. Board game players had significantly less cognitive

decline and less incident depression than non-players. Thus, cognitive decline and depression have the three statistical conditions to be considered as mediating factors [17]: cognitive decline and depression were associated with an increased risk of dementia; board game playing was associated with a reduced risk of cognitive decline and depression; and after multivariate analysis, playing board games was no longer significantly associated with dementia, unlike MMSE score and depression at baseline. This means that playing board games seems to have a favourable effect on cognition and depression before dementia and could therefore have a favourable effect on the risk of dementia. Of course, we cannot exclude that an unmeasured cognitive decline before baseline could precede the discontinuation of board game playing. The relationship could be bidirectional. Only repeated measures of board game playing along with repeated measures of depression and cognition could disentangle this relationship.

Several explanations could be given to explain the relationship between board game playing, cognitive decline, depression and then dementia. Less board game playing might be an early marker or an early consequence of dementia that precedes the decline in MMSE score and the occurrence of depression before dementia. Another explanation could be that board game playing is a marker of behaviour that promotes successful aging, and that this could be the real non-specific factor protecting against cognitive decline, depression and then dementia [18].

Alternatively, board game playing might increase or preserve cognitive reserve, thereby delaying the clinical onset of dementia [1] or slowing the pathological process of the disease [10].

Because of the observational nature of our study, there is a possibility of residual or unmeasured confounding. For example, we did not adjust on genetic factors, which are available only in a small number of the Paquid subjects. However, to our knowledge, there is no evidence showing that APOE4 carriers play board game less than non-carriers, and there is no obvious plausible biological explanation for such an association. The observed association between board game playing and dementia appears to be independent from educational level and marital status, which may influence people's involvement in board game playing.

Our study has other limitations. Although standard criteria and well-established procedures were used to make the diagnoses, misclassification is inevitable. Only reported regular activities were collected at baseline without direct measurement, although the history was checked by informants whenever possible. We had no precise data on the frequency and duration of board game playing. The refusal rate during the follow-up of the cohort was quite

low, but many more subjects died than became demented. However, the risk of death was lower in players than in non-players. Even if a competitive risk between death and dementia might occur, it would lead to an underestimation of the risk of dementia in non-players.

With a long follow-up, this epidemiological study suggests that playing board games has a protective effect on cognitive decline, depression and then dementia. But, this effect appears to be based on cognitive loss at the time of baseline assessment in those who were becoming demented. A reverse causation remains possible. Only controlled studies could truly establish whether playing board games is beneficial and could rule out a reverse causation. However, such a trial appears almost impossible to organize without the possibility of blinding. Even if the evidence is not completely documented, the immediate pleasure procured by playing board games, the advantages that social interaction offers and the ease of applying such a measure in the real world without any drawbacks mean that this activity could be promoted for successful aging.

Acknowledgments and Funding The Paquid study was founded by Novartis pharma, IPSEN pharma, Conseil Régional d'Aquitaine and Institute for European expertise in physiology

Competing interests No competing interests

Contributor statement

JFD was involved in the design, data collection, analysis, he advised on data interpretation and wrote the initial draft. AFS was involved in analysis and she advised on data interpretation. MLG was involved in data collection, analysis and she advised on data interpretation. MV advised on data interpretation. HA was involved in the design and data collection. JMO was involved in the design and data collection. PBG was involved in design and data collection. CH was involved in design, data collection, analysis and she advised on data interpretation. All authors read and approved the final manuscript.

Patient consent Obtained

Ethics approval Ethics approval was provided by the Bordeaux 2 University Ethics Committee in 1988.

Data Sharing JF Dartigues declare that the data for this article are available if required.

References

1. Stern, Y., *Cognitive reserve in ageing and Alzheimer's disease.* Lancet Neurol, 2012 **11**(11): p. 1006-12.
2. Akbaraly, T.N., et al., *Leisure activities and the risk of dementia in the elderly: results from the Three-City Study.* Neurology, 2009. **73**(11): p. 854-61.
3. Stern, Y., et al., *Space Fortress game training and executive control in older adults: a pilot intervention.* Neuropsychol Dev Cogn B Aging Neuropsychol Cogn, 2011. **18**(6): p. 653-77.
4. Barnes, D.E., et al., *Computer-based cognitive training for mild cognitive impairment: results from a pilot randomized, controlled trial.* Alzheimer Dis Assoc Disord, 2009. **23**(3): p. 205-10.
5. Cohen, G.D., et al., *The first therapeutic game specifically designed and evaluated for Alzheimer's disease.* Am J Alzheimers Dis Other Demen, 2008. **23**(6): p. 540-51.
6. Bosch-Domenech, A., R. Nagel, and J.V. Sanchez-Andres, *Prosocial capabilities in Alzheimer's patients.* J Gerontol B Psychol Sci Soc Sci, 2010. **65B**(1): p. 119-28.
7. Clarkson-Smith, L. and A.A. Hartley, *The game of bridge as an exercise in working memory and reasoning.* J Gerontol, 1990. **45**(6): p. P233-8.
8. Nouchi, R., et al., *Brain training game improves executive functions and processing speed in the elderly: a randomized controlled trial.* PLoS One, 2012. **7**(1): p. e29676.
9. Fabrigoule, C., et al., *Social and leisure activities and risk of dementia: a prospective longitudinal study.* J Am Geriatr Soc, 1995. **43**(5): p. 485-90.
10. Verghese, J., et al., *Leisure activities and the risk of dementia in the elderly.* N Engl J Med, 2003. **348**(25): p. 2508-16.
11. Hughes, T.F., et al., *Engagement in reading and hobbies and risk of incident dementia: the MoVIES project.* Am J Alzheimers Dis Other Demen, 2010. **25**(5): p. 432-8.
12. Dartigues, J.F., et al., *[The Paquid research program on the epidemiology of dementia. Methods and initial results]*. Rev Neurol (Paris), 1991. **147**(3): p. 225-30.
13. Folstein, M.F., S.E. Folstein, and P.R. McHugh, *"Mini-mental state". A practical method for grading the cognitive state of patients for the clinician.* J Psychiatr Res, 1975. **12**(3): p. 189-98.
14. Fuhrer, R., et al., *Depressive symptomatology and cognitive functioning: an epidemiological survey in an elderly community sample in France.* Psychol Med, 1992. **22**(1): p. 159-72.
15. Proust-Lima, C., J.F. Dartigues, and H. Jacqmin-Gadda, *Misuse of the linear mixed model when evaluating risk factors of cognitive decline.* Am J Epidemiol, 2011. **174**(9): p. 1077-88.
16. Amieva, H., et al., *Prodromal Alzheimer's disease: Successive emergence of the clinical symptoms.* Ann Neurol, 2008 **64**(5): p. 492-498.
17. Baron, R.M. and D.A. Kenny, *The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations.* J Pers Soc Psychol, 1986. **51**(6): p. 1173-82.
18. Dartigues, J.F. and C. Feart, *Risk factors for Alzheimer disease: aging beyond age?* Neurology, 2011. **77**(3): p. 206-7.

Figure 1. Probability of survival without dementia according to regular board game playing. Kaplan Meier Estimates.

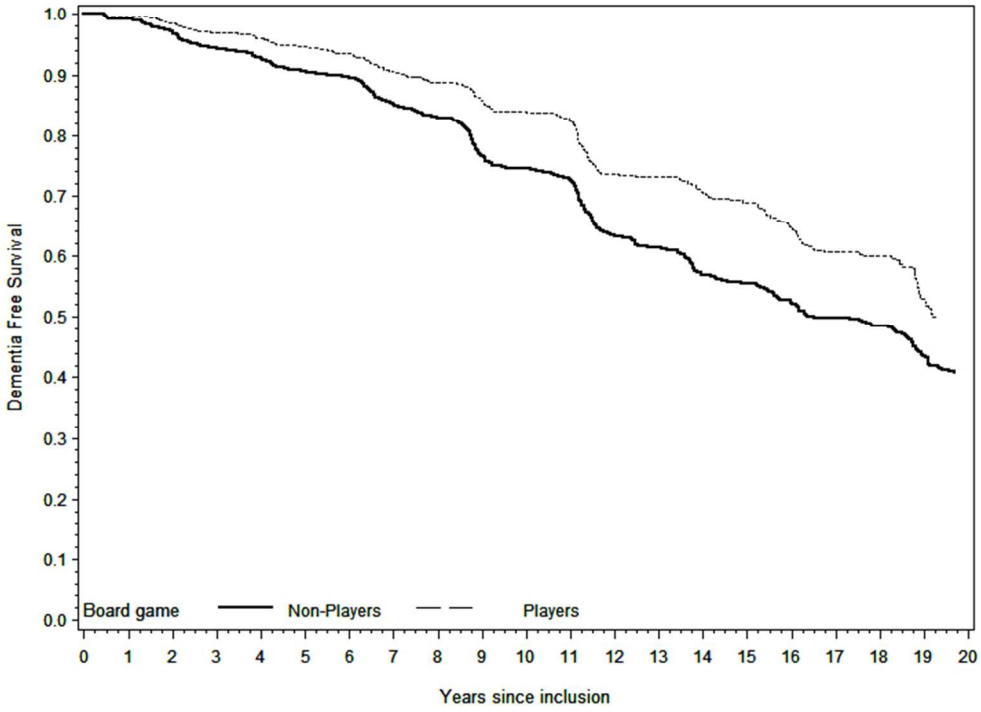

Figure 1. Probability of survival without dementia according to regular board game playing. Kaplan Meier Estimates.
184x151mm (100 x 100 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

Please fill out the page numbers on this form and upload the file as a supplemental file when you submit your revision

Manuscript Number_____

	Item No	Recommendation	Indicate page number ↓ (Or n/a if not applicable)
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	5-6
		(*c*) Explain how missing data were addressed	NA
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6-7
		(b) Indicate number of participants with missing data for each variable of interest	6
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	7
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA
		Cross-sectional study—Report numbers of outcome events or summary measures	NA
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95%	8-9

		confidence interval). Make clear which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Title : Playing board games, cognitive decline and dementia: a French population-based cohort study

Authors : Jean François Dartigues[1], Alexandra Foubert-Samier[1], Mélanie Le Goff[1], Mélanie Viltard[2], Hélène Amieva[1], Jean Marc Orgogozo[1], Pascale Barberger-Gateau[1], Catherine Helmer[1]

Adresses : 1 INSERM U 897, Université Bordeaux Ségalen, 146 rue Léo Saignat, 33076 Bordeaux cedex, France

2 IEEP, Institute for European expertise in physiology, 21, rue Leblanc 75015 Paris, France

Corresponding author : Jean François Dartigues, INSERM U 897, Université Bordeaux Ségalen, 146 rue Léo Saignat, 33076 Bordeaux cedex, France
Tel : +33 5 57571596 Fax : +33 5 57571486
Email : jfd@isped.u-bordeaux2.fr

Key words : Dementia, epidemiology, board games, risk factors, mediating factors

Word count : 2,846 words

Abstract

Objectives: To study the relationship between board game-playing and risk of subsequent dementia in the Paquid cohort.

Design: A prospective population-based study.

Setting: in the Bordeaux area in South Western France.

Participants: 3,675 non-demented subjects at baseline.

Primary outcome measure: the risk of dementia during the twenty years of follow-up.

Results: Among 3,675 non-demented subjects at baseline, 32.2% reported regular board game playing. Eight hundred and forty subjects developed dementia during the twenty years of follow-up. The risk of dementia was fifteen per cent lower in board game players than in non-players (Hazard Ratio =0.85; 95% Confidence Interval = 0.74-0.99; p=0.04) after adjustment on age, gender, education and other confounders. The statistical significance disappeared after supplementary adjustment on baseline MMSE and depression (HR=0. 96; 95% CI = 0.82-1.12; p=0.61). However, board game players had less decline in their MMSE score during the follow-up of the cohort (β=0.011, p=0.03) and less incident depression than non-players (HR=0.84; 95%CI=0.72-0.98; p<0.03).

Conclusions: A possible beneficial effect of board game-playing on the risk of dementia could be mediated by less cognitive decline and less depression in elderly board game players.

Article summery

Article focus:

- Stimulating leisure activities are considered as possible protective factors against dementia and cognitive decline in elderly people, particularly due to enhancement of cognitive reserve.
- Previous papers have shown that playing games can improve cognitive performances in healthy elderly subject, but controversial results were obtained in dementia. Thus, playing board games could be a particularly relevant way to preserve cognition and to prevent cognitive decline or dementia, and could be recommended without any real drawbacks provided the favourable relationship between playing games and dementia is confirmed.
- However, to our knowledge, few authors have studied the relationship between playing board games and the risk of subsequent dementia in prospective cohort studies.

Key messages:

- Using the Paquid cohort data with 20 years of follow-up, we now show that board game players have a 15% lower risk of developing dementia than non-players.
- This reduce risk does not seem to be only a short-term effect as previously reported but is also a long-term effect with a reduction observed one or even two decades after baseline collection of this popular leisure activity. However, in our study, the relationship disappeared after adjustment on baseline cognition and depression, which are known to be strong predictors of dementia.
- A possible beneficial effect of board game-playing on the risk of dementia could be mediated by less cognitive decline and less depression in elderly board game players.

Strengths and limitations:

- With 20 years of follow-up, the Paquid cohort study is one of the longest duration of follow-up in the world for a population-based cohort.
- Because of the observational nature of our study, there is a possibility of residual or unmeasured confounding such as genetic factors.
- Although standard criteria and well-established procedures were used to make the diagnoses, misclassification is inevitable. Only reported regular activities were collected at baseline without direct measurement, although the history was checked by

informants whenever possible. We had no precise data on the frequency and duration of board game playing.

Stimulating leisure activities are considered as possible protective factors against dementia and cognitive decline in elderly people, particularly due to enhancement of cognitive reserve [1-2]. Cognitive reserve is considered as one of the major explanations for differences between individuals in susceptibility to age-related brain changes and pathology related to Alzheimer's disease. Individuals with a large cognitive reserve can tolerate more of these changes than others and maintain their functions [1]. Playing board games is one of the most stimulating leisure activities for elderly people, even at an advanced age, and it has specific advantages compared to other games or activities. Playing board games is a recreational activity that promotes exposure to novelty, taking initiatives, planning, adaptation to winning or losing, and brings immediate pleasure to participants. In addition, playing games is an activity that can be undertaken with family members or friends and even with strangers, and it promotes social interaction and exchange with different generations. Furthermore, it is an inexpensive leisure activity that involves a wide range of tasks from simple ones as in bingo to complex ones as in bridge, and such games can be adapted to the level of the players. Finally, elderly people with physical disability, mild hearing or visual impairment can continue to participate in this stimulating leisure activity, irrespective of the season or the weather. Other stimulating leisure activities like reading, travelling, gardening, doing odd jobs or playing sports do not offer the same advantages and ease of practice. Thus, playing board games could be a particularly relevant way to preserve cognition and to prevent cognitive decline or dementia, and could be recommended without any real drawbacks provided the favourable relationship between playing games and dementia is confirmed.

Previous papers have shown that playing games can improve cognitive performances in healthy elderly subjects [3], but controversial results were obtained in mild cognitive impairment [4] or in dementia [5-6]. Playing games is known to enhance cognitive performances in working memory, executive function, semantic memory and logical reasoning [3, 7-8]. However, to our knowledge, few authors have studied the relationship between playing board games and the risk of subsequent dementia in prospective cohort studies.

In a previous paper on the Paquid population-based cohort, we found that playing board games was significantly associated with a reduced risk of incident dementia three years later [9]. However, the results were obtained after a short follow-up and the significance disappeared after adjustment on cognitive performances at baseline. Similar results were obtained after 20 years of follow-up by Verghese et al in the Bronx Aging Study [10]. On the

contrary, in the MoVIES project, Hughes et al [11] studying different types of games found that only doing crossword puzzles was associated with a reduced risk of dementia while other games like bridge, other card games and other board games were not. Thus, the relationship remains uncertain and more evidence is needed to support preventive recommendations to elderly people about playing board games.

With the prolonged follow-up of the Paquid study with repeated measures of cognition, depression and clinical dementia, we re-analysed the relationship between playing board games collected at the baseline screening of the participants and the occurrence of dementia during the 20 years of follow-up of the cohort. Moreover, we analysed whether depression and cognitive decline before dementia could mediate the relationship between playing board games and dementia.

Methods

Study population

The data came from the Paquid cohort, an epidemiological prospective study on cerebral and functional aging with over 20 years of follow-up. The methodology has been previously described [12]. In brief, the initial baseline sample included 3,777 community dwellers, aged 65 or more, randomly selected from the electoral rolls in 75 different sites of two French administrative districts (Departments of Gironde and Dordogne). The participants were representative of the elderly community dwellers of the area in terms of age and sex. Since the baseline visit in 1988, the participants have been revisited at home by a dedicated neuropsychologist up to nine times over the entire follow-up. After 22 years, the Paquid cohort is still ongoing. The present analyses were conducted on the data collected over a 20-year period of follow-up.

Data collection

Leisure and social activities were collected at baseline by a standardized questionnaire during a face-to-face interview conducted by a psychologist. Ten activities were explored with the question: “Do you usually undertake this activity (at least once a week): yes or no?” The following activities were screened: reading, gardening, doing odd jobs or knitting, watching television, participating in sports, playing board games, looking after children, participating in group activities or associations, visiting friends or family members and travelling. Only playing board games was considered in this paper. Board games comprised card games, bingo, chess, draughts and other parlour games.

A neuropsychological battery was conducted at baseline and at each follow-up visit with assessment of visual memory, verbal memory, language, executive function and simple logical reasoning [12]. A French version of the Mini-Mental State Examination (MMSE) [13] was used as an index of global cognitive performance. Scores range from 0 to 30. Depressive symptomatology was assessed at each follow-up screening using the French version of the Centre for Epidemiological Studies Depression Scale (CES-D) [14]. This is a 20-item self-report scale developed for use in epidemiological studies in the community. Scores range from 0 to 60 according to the frequency of the depressive symptoms during the previous week. According to a previous validation study for the French population, CES-D cut-off scores of 17 for men and 23 for women indicate clinically relevant depression [14]. Subjects were considered as having depression if they were treated by anti-depressors or had a score above the cut-off score at the CESD.

At baseline and at each follow-up visit, after the neuropsychological evaluation, the neuropsychologist filled in the Diagnostic and Statistical Manual of Mental Disorders 3rd ed. revised (DSM-IIIR) to identify subjects suspected of being demented. These cases and those with at least a three-point decline in MMSE score since the previous visit were examined at home by a neurologist to confirm or not the diagnosis of dementia and specify the etiology. All diagnoses of dementia were assigned at a case consensus conference attended by the study neurologist and two other dementia specialists according to the DSM-IIIR criteria. When evaluating cognitive status, the members of the consensus conference had no knowledge of leisure activities practiced by subjects.

Statistical analyses

Descriptive and comparative analyses were conducted using appropriate tests (*t*-test or chi-square test). Kaplan-Meier curves for the risk of incident dementia were obtained for the two categories of subjects according to their board game playing and compared with the Log Rank test.

To estimate the risk of dementia associated with game-playing, incident cases of dementia occurring between the baseline screening and the 20th year of follow-up were considered as an outcome variable. The time-to-event was defined as the time from baseline to the date of a diagnosis of dementia or to the last follow-up for subjects without dementia. Participants were censored at the time of diagnosis of dementia or at the last follow-up for those non-demented. Adjustment on possible confounders was performed with the multivariate Cox proportional hazards model with delayed entry taking age as time scale**.** The

multivariate model included the following covariates: gender, educational level (classified in five levels: high school, college, secondary level, primary school with diploma, primary school without diploma or no schooling), marital status, self-reported diabetes and stroke (model 1). Supplementary adjustment was made on self-reported visual, hearing impairment and ApoE 4 genotype on the subsample of the cohort with blood sampling (n=623).

We examined the influence of baseline cognitive performances on the MMSE score and the presence of depression at baseline (model 2). Risk of cognitive decline was analysed by a multivariate mixed model taking repeated values of the MMSE score during the 20 years of follow-up as outcome. Beta transformation of the MMSE score was used to take into account the ceiling effect of the test in non-demented cases [15]. Board game playing was considered as covariate with adjustment on confounders as in the previous multivariate model.

To estimate the risk of incident depression associated with board game-playing, incident cases of depression occurring between the baseline screening and the 20th year of follow-up were considered as the outcome variable. The time-to-event was defined as the time from baseline to the date of a diagnosis of depression or to the last follow-up for subjects without depression. Participants were censored at the time of the first diagnosis of depression during the follow-up or at the last follow-up for those never depressed over the follow-up. Adjustment on possible confounders was performed with the multivariate Cox proportional hazards model using the same adjustments as previously.

The analyses were performed using SAS, version 9.2 (SAS Institute, Inc., Cary, NC).

Results

Characteristics of board game players

Among the 3,777 participants, 102 (2.7%) were classified as prevalent cases of dementia at the baseline screening and excluded from the sample. Of the remaining 3675 subjects, five had missing data for board game playing (0.1%). One thousand one hundred and eighty-one subjects reported regular board game playing (32.2%). Board game players were younger, more educated, more often married, less depressed and had better cognitive performances at baseline screening than non-players (Table 1). However, the proportion of board game players remained high in very old age (18% in subjects aged from 85 to 89 years, and even 12.5% in those older than 89 years), and even in non-demented subjects with low cognitive performances (18.8% in subjects with an MMSE between 20 and 23, 10.6% in subjects with an MMSE lower than 20). In the subsample of 623 subjects with blood sampling

the proportion of ApoE 4 carriers was the same in both groups (23.5% for non-players vs 21.2 for players %, p=0.5).

Table 1. Characteristics of participants according to board game playing. Paquid Study n=3670

	Players (n=1181)	Non-players (n=2489)	p value
Gender (males)	501 (42.4)	1039 (41.7)	0.70
Age at inclusion (years): mean (SD)	73.6 (5.9)	76.0 (7.1)	<0.0001
Educational Level (higher)			
Primary school without diploma or no schooling	302 (25.6)	976 (39.2)	
Primary school with diploma	546 (46.2)	1058 (42.5)	
Secondary level	179 (15.2)	228 (9.2)	<0.0001
College	77 (6.5)	127 (5.1)	
High school	77 (6.5)	100 (4.0)	
Marital Status			0.0305
Married	708 (59.9)	1394 (56.0)	
Widowed	381 (32.3)	905 (36.4)	
Single	52 (4.4)	127 (5.1)	
Divorced	40 (3.4)	63 (2.5)	
Diabetes	87 (7.4)	219 (8.8)	0.14
Stroke	42 (3.6)	152 (6.1)	0.0012
MMSE score at inclusion: mean (SD)	26.9 (2.6)	25.3 (3.6)	<0.0001
Depression at inclusion	116 (9.9)	494 (20.4)	<0.0001
ApoE 4 genotype (carriers)*	48 (21.2)	93 (23.5)	0.5

Unless otherwise stated values are numbers (%)

SD: Standard Deviation

* n= 623 (396 non-players and 227 players)

Board game-playing and risk of incident dementia

Among the 3670 participants, 2987 (81.4%) were seen again at least once during the twenty years of follow-up. One hundred and forty-two persons deceased before the first screening (3.9%) and 541 refused to participate or were lost to follow-up (14.7%). The proportion of board game players was greater in those who were followed-up at least once.

Eight hundred and thirty cases of incident dementia (27.8%) were observed during the twenty years of follow-up. The cumulative risk of dementia was significantly reduced in subjects board game players versus non-players (Log rank test = 24.2, p<0.001). After three years of follow-up, 3% of board players developed dementia versus 6% of non-players, 16% versus 27% after ten years and 47% versus 58% after twenty years (Figure 1).

After adjustment on age, gender, education, marital status, history of stroke and diabetes (Table 2), the risk of dementia remained significantly reduced (HR = 0.85, 95%CI= 0.74-0.99, p=0.04). The relationship remained unchanged after supplementary adjustment on visual and hearing impairment. However, the relationship was no longer significant after supplementary adjustment on depression and MMSE score at baseline (HR=0.96, 95%CI=0.82-1.12, p=0.61). In the latter model, depression (HR=1.34, 95%CI=1.12-1.60, p=0.0011) and MMSE score at baseline (for one point fewer HR=1.10, 95%CI=1.08-1.12, p<0.0001) were strong predictors of dementia. In supplementary analyses, we found that after separated adjustment on MMSE and depression, the significant relationships between board game playing and dementia disappeared in both analyses, but most of the effect seems to be due to controlling for MMSE.

Finally, we made a supplementary adjustment on ApoE 4 genotype on a subsample of the Paquid cohort of 618 subjects. In this subsample of subjects, after adjustment on ApoE 4 genotype (carriers vs no carriers), the HR for dementia related to playing board game decreased to 0.74 but was no more significant (p=0.06).

Table 2. Risk of dementia according to board game playing in the Paquid cohort. Multivariate Cox model.

	Model 1*			Model 2**		
	HR	95%CI	p Value	HR	95%CI	p Value
Board game (players vs non-players)	0.85	0.74-0.99	0.04	0.96	0.82-1.13	0.62
Gender (female vs male)	1.29	1.10-1.52	0.002	1.23	1.04-1.46	0.01
Education (higher vs lower)						
Primary school with diploma	0.65	0.56-0.76	<0.0001	0.85	0.72-1.01	0.07
Secondary level	0.58	0.45-0.74	<0.0001	0.84	0.64-1.11	0.22
College	0.50	0.36-0.71	0.0001	0.76	0.53-1.09	0.13
High school	0.38	0.25-0.58	<0.0001	0.57	0.37-0.88	0.01
marital status						
widowed vs married	0.89	0.76-1.05	0.16	0.85	0.72-1.00	0.05
single vs married	1.28	0.93-1.75	0.12	1.20	0.86-1.68	0.28
divorced vs married	1.16	0.77-1.74	0.49	1.06	0.70-1.61	0.78
history of stroke (yes vs no)	1.55	1.17-2.05	0.0016	1.31	0.97-1.78	0.08
Diabetes (yes vs no)	1.10	0.84-1.46	0.48	1.05	0.79-1.40	0.72
MMSE score				0.91	0.89-0.93	<0.0001
Depression (yes vs no)				1.34	1.12-1.59	0.001

* Adjustment on age, gender, education, marital status, history of stroke and diabetes

** Adjustment on age, gender, education, marital status, history of stroke, diabetes, MMSE score and depression

Board game-playing, cognitive decline and risk of incident depression

Board game players had less cognitive decline in MMSE score than non-players after adjustment on age, gender, education, marital status, history of stroke and diabetes (β=0.011, p=0.03). The relationship remained unchanged after supplementary adjustment on depression at baseline (β=0.010, p=0.04). The cognitive decline may begin several years before the diagnosis of dementia as showed by us [16]. To explore a possible reverse causation, we studied the relationship between board game playing and the cognitive decline, eliminating those who became demented over the first 10 years of follow-up and over the entire period. The beta coefficients slightly decrease (from 0.01 to 0.008) but become non significant

(respectively p=0.07 and p=0.15). However a decrease of statistical power and a selection of the sample could explain these results. At the whole, this supplementary analysis is more in favour of a reverse causation from outcome to exposure.

Among the 2987 participants, 2464 were classified as non-depressed at baseline. Of those, 718 developed incident depression (29.1%) during the 20 years of follow-up. The risk of incident depression was significantly reduced in board game players after adjustment on age, gender, education, marital status, history of stroke and diabetes (HR=0.84; 95%CI=0.72-0.98; p<0.03). This relationship remained almost unchanged but was only borderline significant after adjustment on MMSE score at baseline screening (HR=0.87; 95%CI=0.74-1.02; p=0.08).

Discussion

Playing board games is a common stimulating leisure activity in elderly French people since one third of subjects older than 65 in the general population reported regularly practising it. The rate of such activity remained high even in very old age and in subjects with cognitive deficit. Using the Paquid cohort data with 20 years of follow-up, which is one of the longest duration of follow-up in the world for a population-based cohort, we now show that board game players have a 15% lower risk of developing dementia than non-players. This reduced risk does not seem to be only a short-term effect as previously reported [9] but is also a long-term effect with a reduction observed one or even two decades after the baseline collection of this popular leisure activity. The association between board game playing and the risk of dementia remained robust after adjustment on confounding variables such as age, gender, educational level, marital status, and presence or absence of stroke or diabetes.

Our results are in accordance with findings from the Bronx Aging Cohort [10] conducted in a different population in the USA. However, in our study, the relationship disappeared after adjustment on baseline cognition and depression, which are known to be strong predictors of dementia. This means that the reduced risk of dementia could be related to the fact that board game players had better cognitive performances and were less depressed at baseline screening than non-players. On the contrary, baseline MMSE score and depression appeared to be significantly related to the subsequent risk of dementia.

To test whether cognitive decline and the occurrence of depression were mediating factors in the relationship between playing board games and dementia, we studied non-demented subjects with regard to the risk of cognitive decline and incident depression in board game players versus non-players. Board game players had significantly less cognitive

decline and less incident depression than non-players. Thus, cognitive decline and depression have the three statistical conditions to be considered as mediating factors [17]: cognitive decline and depression were associated with an increased risk of dementia; board game playing was associated with a reduced risk of cognitive decline and depression; and after multivariate analysis, playing board games was no longer significantly associated with dementia, unlike MMSE score and depression at baseline. This means that playing board games seems to have a favourable effect on cognition and depression before dementia and could therefore have a favourable effect on the risk of dementia. Of course, we cannot exclude that an unmeasured cognitive decline before baseline could precede the discontinuation of board game playing. The relationship could be bidirectional. Only repeated measures of board game playing along with repeated measures of depression and cognition could disentangle this relationship.

Several explanations could be given to explain the relationship between board game playing, cognitive decline, depression and then dementia. Less board game playing might be an early marker or an early consequence of dementia that precedes the decline in MMSE score and the occurrence of depression before dementia. Another explanation could be that board game playing is a marker of behaviour that promotes successful aging, and that this could be the real non-specific factor protecting against cognitive decline, depression and then dementia [18].

Alternatively, board game playing might increase or preserve cognitive reserve, thereby delaying the clinical onset of dementia [1] or slowing the pathological process of the disease [10].

Because of the observational nature of our study, there is a possibility of residual or unmeasured confounding. For example, we did not adjust on genetic factors, which are available only in a small number of the Paquid subjects. However, to our knowledge, there is no evidence showing that APOE4 carriers play board game less than non-carriers, and there is no obvious plausible biological explanation for such an association. The observed association between board game playing and dementia appears to be independent from educational level and marital status, which may influence people's involvement in board game playing.

Our study has other limitations. Although standard criteria and well-established procedures were used to make the diagnoses, misclassification is inevitable. Only reported regular activities were collected at baseline without direct measurement, although the history was checked by informants whenever possible. We had no precise data on the frequency and duration of board game playing. The refusal rate during the follow-up of the cohort was quite

low, but many more subjects died than became demented. However, the risk of death was lower in players than in non-players. Even if a competitive risk between death and dementia might occur, it would lead to an underestimation of the risk of dementia in non-players.

With a long follow-up, this epidemiological study suggests that playing board games has a protective effect on cognitive decline, depression and then dementia. But, this effect appears to be based on cognitive loss at the time of baseline assessment in those who were becoming demented. A reverse causation remains possible. Only controlled studies could truly establish whether playing board games is beneficial and could rule out a reverse causation. However, such a trial appears almost impossible to organize without the possibility of blinding. Even if the evidence is not completely documented, the immediate pleasure procured by playing board games, the advantages that social interaction offers and the ease of applying such a measure in the real world without any drawbacks mean that this activity could be promoted for successful aging.

Acknowledgments and Funding The Paquid study was founded by Novartis pharma, IPSEN pharma, Conseil Régional d'Aquitaine and Institute for European expertise in physiology

Competing interests No competing interests

Contributor statement

JFD was involved in the design, data collection, analysis, he advised on data interpretation and wrote the initial draft. AFS was involved in analysis and she advised on data interpretation. MLG was involved in data collection, analysis and she advised on data interpretation. MV advised on data interpretation. HA was involved in the design and data collection. JMO was involved in the design and data collection. PBG was involved in design and data collection. CH was involved in design, data collection, analysis and she advised on data interpretation. All authors read and approved the final manuscript.

Patient consent Obtained

Ethics approval Ethics approval was provided by the Bordeaux 2 University Ethics Committee in 1988.

Data Sharing JF Dartigues declare that the data for this article are available if required.

References

1. Stern, Y., *Cognitive reserve in ageing and Alzheimer's disease.* Lancet Neurol, 2012 **11**(11): p. 1006-12.
2. Akbaraly, T.N., et al., *Leisure activities and the risk of dementia in the elderly: results from the Three-City Study.* Neurology, 2009. **73**(11): p. 854-61.
3. Stern, Y., et al., *Space Fortress game training and executive control in older adults: a pilot intervention.* Neuropsychol Dev Cogn B Aging Neuropsychol Cogn, 2011. **18**(6): p. 653-77.
4. Barnes, D.E., et al., *Computer-based cognitive training for mild cognitive impairment: results from a pilot randomized, controlled trial.* Alzheimer Dis Assoc Disord, 2009. **23**(3): p. 205-10.
5. Cohen, G.D., et al., *The first therapeutic game specifically designed and evaluated for Alzheimer's disease.* Am J Alzheimers Dis Other Demen, 2008. **23**(6): p. 540-51.
6. Bosch-Domenech, A., R. Nagel, and J.V. Sanchez-Andres, *Prosocial capabilities in Alzheimer's patients.* J Gerontol B Psychol Sci Soc Sci, 2010. **65B**(1): p. 119-28.
7. Clarkson-Smith, L. and A.A. Hartley, *The game of bridge as an exercise in working memory and reasoning.* J Gerontol, 1990. **45**(6): p. P233-8.
8. Nouchi, R., et al., *Brain training game improves executive functions and processing speed in the elderly: a randomized controlled trial.* PLoS One, 2012. **7**(1): p. e29676.
9. Fabrigoule, C., et al., *Social and leisure activities and risk of dementia: a prospective longitudinal study.* J Am Geriatr Soc, 1995. **43**(5): p. 485-90.
10. Verghese, J., et al., *Leisure activities and the risk of dementia in the elderly.* N Engl J Med, 2003. **348**(25): p. 2508-16.
11. Hughes, T.F., et al., *Engagement in reading and hobbies and risk of incident dementia: the MoVIES project.* Am J Alzheimers Dis Other Demen, 2010. **25**(5): p. 432-8.
12. Dartigues, J.F., et al., *[The Paquid research program on the epidemiology of dementia. Methods and initial results]*. Rev Neurol (Paris), 1991. **147**(3): p. 225-30.
13. Folstein, M.F., S.E. Folstein, and P.R. McHugh, *"Mini-mental state". A practical method for grading the cognitive state of patients for the clinician.* J Psychiatr Res, 1975. **12**(3): p. 189-98.
14. Fuhrer, R., et al., *Depressive symptomatology and cognitive functioning: an epidemiological survey in an elderly community sample in France.* Psychol Med, 1992. **22**(1): p. 159-72.
15. Proust-Lima, C., J.F. Dartigues, and H. Jacqmin-Gadda, *Misuse of the linear mixed model when evaluating risk factors of cognitive decline.* Am J Epidemiol, 2011. **174**(9): p. 1077-88.
16. Amieva, H., et al., *Prodromal Alzheimer's disease: Successive emergence of the clinical symptoms.* Ann Neurol, 2008 **64**(5): p. 492-498.
17. Baron, R.M. and D.A. Kenny, *The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations.* J Pers Soc Psychol, 1986. **51**(6): p. 1173-82.
18. Dartigues, J.F. and C. Feart, *Risk factors for Alzheimer disease: aging beyond age?* Neurology, 2011. **77**(3): p. 206-7.

Figure 1. Probability of survival without dementia according to regular board game playing. Kaplan Meier Estimates.